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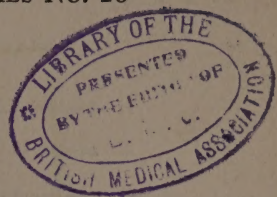


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NERVOUS AND MENTAL DISEASE MONOGRAPH SERIES No. 20



VAGOTONIA

A Clinical Study in Vegetative Neurology

BY
DR. HANS EPPINGER AND DR. LEO HESS
OF VIENNA

AUTHORIZED TRANSLATION BY
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VAGOTONIA¹

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I. INTRODUCTION

It is often unsatisfactory for the physician, when investigating a disease dependent upon long standing disturbance of internal organs, to find that he must be content to make a diagnosis of "Neurosis." The symptomatology and the impossibility of establishing any anatomical basis for the disease always remain the most conspicuous points in formulating the diagnosis of a neurosis of an internal organ. It is true that one would be inclined to correlate these disturbances with nerve abnormalities were it possible to form any clear picture of the significance of

¹Sammlung klinischer Abhandlungen über Pathologie und Therapie der Stoffwechsel und Ernährungstörungen. Herausgegeben von Prof. Dr. Carl von Noorden. Heft 9 u. 10. August Hirschwald, Berlin. 1910.

the nerves either in the normal progress of the functions of organs or in pathological conditions, but when one considers how difficult under such circumstances it is to give a clear definition of the conception of "a nervous disease of an internal organ" one can only recall the truth of the saying that where knowledge is lacking a clue will appear at the right time. If an attempt be made to substitute a precise conception for obscure ideas, special care must be taken to construct such a concept upon a foundation of facts.

Instead of simply making use of the general expression "nervous," which so frequently is nothing more than the expression of a soothing statement, either to the patient or to the physician, we must attempt, where we can, to separate definite disease pictures from an etiological point of view. Just as we may analyse with precision the diseases of the cerebrospinal nerves, in the light of anatomical and physiological knowledge, so, when diagnosing diseases of the nerves which supply internal organs, we must attempt to direct our thoughts along anatomical and physiological channels. Above all, if one really wishes to make further progress, it is necessary to review the physiological facts with thoroughness. It is through an exact knowledge of physiology that one may justly introduce pathology and apply it to the analysis of disease.

2. THE VEGETATIVE NERVOUS SYSTEM AND ITS RELATION TO DRUGS

In contrast to the "Animal" (sensori-motor) nervous system which serves the senses and the muscles controlled by the will, we include under the term "Vegetative" nervous system all those nerve fibers which go to organs having smooth muscles, such as the intestines, blood vessels, gland ducts and skin, as well as the nerve structures which exert a secretory influence upon glands. Besides these organs, there are to be included certain cross-striated muscles: as the heart, the beginning and end of the alimentary canal, and the muscles of the genital apparatus. With the exception of the heart, all of these muscles are functionally very similar to smooth muscles.

The vegetative nervous system cannot be readily distinguished anatomically from the sensori-motor nervous system,

because their nuclei lie close to one another both in the brain and spinal cord, and because their fibers have many anastomoses with each other. The principal difference lies in the peripheral make-up of the two systems. The nerves of the sensori-motor system have but one neurone between the nerve centers and the cross-striated muscles, whereas the nerves which go from the spinal axis to involuntary organs of vegetative nature have ganglion cells interposed in their course. Since both afferent and efferent fibers are interrupted, the path from the central nervous system to its organ may be divided into preganglionic and postganglionic segments. The ganglionic interruptions vary in their location. In some cases they are in the sympathetic cord, in some on the path from this cord to the periphery, as, for example, in the celiac ganglion; in some at the periphery itself, as in the case of the heart and intestines. Langley divides these ganglia, on topographic grounds, into ganglia of the first, second and third order.

The uniformity of the anatomic arrangement of the vegetative system foreshadows a uniform pharmacologic reaction, and it is this pharmacologic uniformity which has made possible the separation of the vegetative from the sensori-motor nervous system. If vegetative nerves are stimulated peripheral to their origin in the central gray of the cord, definite manifestations are obtained. These may be eliminated at once if nicotine is painted upon the ganglion between the site of stimulation and the periphery. The functional manifestations of the activity of the sensori-motor nerves are on the contrary unaffected by nicotine.

The vegetative nervous system may be divided anatomically as well as functionally. The system of fibers which arises from the middle and lower part of the thoracic cord and from the upper part of the lumbar cord forms an anatomical entity, which ramifying distally makes up the sympathetic cord. Distal to this it is scarcely possible to distinguish the sympathetic fibers anatomically, since they pass to their substations commingled with other nerve fibers.

The second anatomical grouping includes the fibers which arise in part from the brain and medulla, in part from the sacral part of the spinal cord. These do not come into any relation with the sympathetic cord. From the view point of gross

anatomy this system may be further divided into three parts: [a] Midbrain, [b] Bulbar, [c] Sacral.

The nerve plexus from the midbrain segments finds egress, in the main, by way of the oculomotor nerve pathways. Its fibers are interrupted in the ciliary ganglia and subserve certain definite functions of the eye. The nerves from the bulbar segments proceed in part by way of the facial and glossopharyngeal nerves to supply fibers to the glands and vasodilators of the head. But the largest and most important branch of this segment is the vagus, the principal nerve of the viscera. It supplies the heart, bronchi, esophagus, stomach, intestine and pancreas. The nerves from the sacral segment are contained in the pelvic nerve. This supplies the descending colon, the sigmoid, anus, bladder, and genital apparatus.

From this classification it may be seen that all of the vegetative organs are supplied not only by the nervous network which passes through the sympathetic cord, but also by nerve fibers which come from the other system. An exception to this rule is found in the sweat glands, pilomotor muscles, and vascular muscles of the viscera. These, as far as can be discovered anatomically, are only supplied by fibers from the sympathetic cord.

For brevity's sake, it is customary to speak of all nerves which arise from the sympathetic cord as "*sympathetic*," while all other vegetative nerves of the nervous system are spoken of as "*autonomic*" [the system of the "extended vagus"].

Electrical investigations have already shown that in many organs the manifestations caused by stimulation of the fibers of one system may be abolished when stimulation is applied to the corresponding fibers of the other.

These reactions show that many physiological antagonists may be demonstrated in the two systems. But the fact that the different nerves of the two systems may be commingled on their way to their end-organs makes anatomical differentiation impossible and physiological testing extremely difficult.

In certain pharmacological substances on the contrary, a means of getting at this differentiation is found. Adrenalin is known to be a substance which acts solely upon the "*sympathetic*" nervous system. Its action is similar to that of electrical stimulation of the sympathetic fibers [Table I]. One may,

therefore, always regard a manifestation of the action of adrenalin as equivalent to that of stimulation of "sympathetic" fibers.

The "autonomic" nervous system can also be influenced exclusively by certain drugs. The most important of these are atropin, pilocarpin, physostigmin, and muscarin. Following the use of muscarin, pilocarpin, or physostigmin, the same effects may be produced as are obtained by stimulation of autonomic fibers. Atropin, on the other hand, prevents many of the effects which are caused by stimulation of the autonomic fibers. It is to be expected, therefore, that atropin would be able to counteract, to a certain degree, the effects produced by pilocarpin, muscarin, and physostigmin. Experimentally this may be shown to be the case.

The parallelism between physiological stimulation and the pharmacological action of these selectively acting drugs seems to be broken by the peculiar behavior of the sweat glands. While the results of anatomical and physiological investigations make it seem probable that these glands are innervated by the sympathetic, yet they react to autonomic poisons, whereas the sympathicotonic adrenalin is able to abolish the secretion of the sweat glands.

Since pharmacological tests seem to be the most decisive, the innervation of the sweat glands must be regarded as of autonomic origin.

Before proceeding further, a tabular résumé of the antagonism of the action between adrenalin on the one hand, and of atropin and pilocarpin on the other is here presented.

A detailed review of the literature cannot be given here owing to the great abundance of facts. This table has been partly taken from the work of Froehlich and Loewi,² in part from the work on Internal Secretions by Arthur Biedl.³

These tables are chiefly of service in showing that pharmacological investigations particularly have confirmed the idea that the two nervous systems, sympathetic and autonomic, are antagonistic in their action. While adrenalin exerts equal action upon nearly all organs with sympathetic innervation, it may be seen, however, that pilocarpin has more action on some parts of

² Arch. f. Exp. Path. u. Pharm., Vol. 59, p. 34.

³ Vienna, 1910 (2d edit., 1914), English translation, Wm. Wood & Co., New York. See also Higier on the Vegetative Nervous System in preparation for Monograph Series, now appearing in the Jour. of N. & M. Dis. Vol. 4 et seq.

Action of Stimulation of the Sympathetic System	Action of		Organ	Action of		Action of Stimulation of the Autonomic System
	Atropin	Adrenalin		Pilocarpin	Ergotoxin	
Stim. (Th. I-II)	Para.	Stim.	Sphincter iridis	Stim.	—	Stim. (N. III)
Stim. (Th. I-III)	Para.	Stim.	Dilator iridis	Stim.	—	Stim. (N. III)
Stim. (Th. II-IV)	Para.	(Stim.?)	Ciliary muscle	Para.	Para.	Ch. tympani. secretion
Constrict. (Th. II-IV)	Constrict.?	Constriction	Orbital muscle	Stim.	—	Dilat. (N. X)
Constrict. (Th. II-LIV)	Dilatation	Dilatation	Salivary glands	—	—	Constrict. (N. IX)
Constrict. (Th. II-L, IV)	Constrict.?	Constriction	Cortical blood vessels	—	—	—
Stim. (Th. II-L, IV)	Dilatation	Dilatation	Buccal blood vessels	—	—	—
Stim. (Th. IV-VII)	Constriction	Constriction	Skin blood vessels, head region	Constrict.	—	—
Stim. (Th. I-V)	Inhib.	Inhib.	Coronary blood vessels	—	Dilatat.	Dilat. (N. pelv.)
Relax. (Th. II-V)	Stim.	Stim.	Intestinal blood vessels	—	—	—
Para. (Th. II-L, IV)	Relax.	Relax.	Genital blood vessels	Stim.	—	—
Diminished (Th. II-L, IV)	Para.	Para.	Sweat glands	Inhib.	Para.	Inhib. (N. X)
Diminished?	Diminished	Diminished?	Pilomotor muscles of the face	Stim.	Inhib.	Stim. (N. X)
Inhibition (Th. II-L, IV)	Para.	Para.	Heart muscle	—	—	Stim. (N. X)
Relax. (L. I-IV)	Relax.	Relax.	Esophagus	Increase	—	Increases (N. X)
Relax. (L. I-IV)	Relax.	Relax.	Cardia	Increase	—	Increases (N. X)
Relax. (Th. II-L, IV)	Relax.	Relax.	Gastric tone	Increase	—	Increases (N. X)
Inhib.?	Inhib.	Inhib.	Gastric peristalsis	Stim.	—	Stim. (N. X)
Contract. (L. I-IV)	Contract.	Contract.	Small intestine peristalsis	Spasm	—	Stim. (N. pelv.)
Relax. (L. I-IV)	Relax.	Relax.	Colon	Contract.	—	Spasm (N. pelv.)
Contract. (L. I-IV)	Contract.	Contract.	Sphincter ani (muscle)	Stim.	—	Contract. (N. X)
Relax. (L. I-IV)	Relax.	Relax.	Gall-bladder	Stim.	—	Stim. (N. X)
Contract. (L. I-IV)	Contract.	Contract.	Pancreatic secretion	—	—	Relax. (N. pelv.)
Relax. (L. I-IV)	Relax.	Relax.	Bronchial muscle	Relax.	—	Contract. (N. pelv.)
Contract. (L. I-IV)	Contract.	Contract.	Sphincter vesicæ	—	—	—
Relax. (L. I-IV)	Relax.	Relax.	Detrusor vesicæ	Relax.	—	—
Contract. (L. I-IV)	Contract.	Contract.	Uterus (Preg.)	Contract.	—	—
Relax. (L. I-IV)	Relax.	Relax.	Uterus (Non-preg.)	—	—	—
Contract. (L. I-IV)	Contract.	Contract.	M. retractor penis	—	—	—
Pigûre	Raised	Raised	Carbohydrate tolerance	Diminished	—	—
Heat puncture	Contract.	Contract.	Heat balance	—	—	—
Contract.	—	—	Pigment cells	Dilat.?	—	—

Stim. = stimulation. Constrict. = constriction. Relax = relaxation. Para. = paralysis. Inhib. = inhibition.

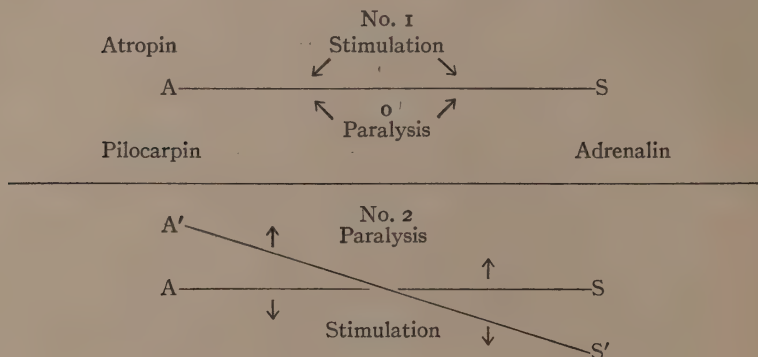
the autonomic system than on others. From this it may be seen that its effects cannot be contrasted with the universal effects of the action of adrenalin. Atropin also shows gradual differentiation in its action, since it has practically no action upon the pelvic nerve, while it exerts a powerful influence upon the cranial portion of the autonomic system. Other drugs are known which also have a powerful action upon the autonomic, more in some of its branches than in others. Pilocarpin itself acts particularly upon secretory autonomic fibers, while its action upon the heart is much less potent. This gradual differentiation is very evident if one compares the action of pilocarpin upon the heart with that of muscarin. What is emphasized in considering these two autonomic stimulants, muscarin and pilocarpin, is that their selectivity differs. In the case of the heart, for example, muscarin may cause cessation of its action, while pilocarpin and physostigmin, with the exception of a transitory slowing of the pulse, have no noteworthy effect. That these drugs do influence the cardiac branches of the vagus, however, is shown by stimulating that nerve. Thus the effect of a stimulus applied to the heart is enormously increased after the administration of physostigmin, so much so that even a mild stimulation may cause the heart to stop beating.

These few examples serve to show that the various autonomic stimulants do not have precisely similar effects, but have greater affinities for certain branches than for others, and furthermore, it is worth noting that some autonomic poisons affect the central more than the peripheral endings. Picrotoxin is an example. Finally a differentiation must be made between drugs which act as direct stimulants, and those which act by increasing the irritability, i. e., the reactivity to other stimuli. Of the latter physostigmin is an example.

In order to determine many physiological and pharmacological questions it would be of great value to have some substance which would act as a paralyzant for the sympathetic system. Opinions upon ergotoxin are divided. At any rate, it is not a drug which can be used as the desired substance for testing the sympathetic. To a certain degree, at least, it may be expected that paralysis of the sympathetic will give symptoms similar to those of stimulation of the autonomic. Thus, pilocarpin, a stimulant of the

autonomic may to a certain extent be regarded as a paralyzant of the sympathetic. The symptomatic contrast of sympathetic paralysis and autonomic stimulation on the one hand with sympathetic stimulation and autonomic paralysis on the other may best be seen in the pupillary reactions to these different poisons.

The following diagram shows these relations:



In these diagrams, A S represents a balance with arms of equal length, showing the equilibrium in the tonus of the two systems. A = autonomic, S = sympathetic. If there be stimulation at S, say by adrenalin, the balance will tilt towards paralysis on the A side, as shown in diagram 2. Also, if a weight be taken from A, it will rise as in diagram 2.

Thus it may be seen how atropin and adrenalin may produce the same effects in the body, and also how pilocarpin may produce symptoms similar to those of paralysis of the sympathetic.

3. TONUS AND THE DEFINITION OF THE TERM VAGOTONIA

It is of great physiological interest that the stimulant of the sympathetic nervous system—adrenalin—is produced by almost all vertebrates, and that it lies in close anatomical relationship to the sympathetic system. It is formed just where it exerts its greatest action, since the so-called chromaffin cells, the adrenalin forming cells, accompany the sympathetic in its course. Through the investigations of Ehrmann, we know that adrenalin is continuously flowing from the adrenals and thus exerts a continuous influence upon the sympathetic. From this it must be concluded that the stimulating effect of the sympathetic upon

its end organs is not an intermittent one, only produced when the affected organs become active, but is in reality continuous.

It is probable that a similar state exists with reference to the autonomic system and that a specific analogue to adrenalin, an "autonomin," exists even though it is not known at present. Substitutes for this are found in certain poisons which have been mentioned—pilocarpin and physostigmin. These drugs act exclusively upon the autonomic system.

In this sense these two substances are valuable substitutes for the supposed physiological "autonomin." The study of pharmacological substances shows that vagotropic and sympathotropic activities do not always exert a universal action, but have a special predilection for one or another branch of the two systems. If one recalls that certain physiological hormones, as pituitrin, have also but a selective action on certain parts of one or the other vegetative nervous systems, it is easy to conceive that similar conditions exist in the body, and that many hormones may have definite relations only to a special branch of the two nervous systems.

In studying the interrelations of the activities of the endocrinous glands, it is found, for instance, that the organ which produces adrenalin, the chromaffin system, receives inhibitory influences from the pancreas, since following the extirpation of the pancreas, the chromaffin system (adrenalin) takes the upper hand.⁴ On the other hand a defect or deficiency of the chromaffin system will permit the autonomic system to increase its activity. This, for example, is seen in Addison's Disease. The inhibitory as well as the excitatory impulses which are produced by over or under activity on the part of any gland of internal secretion, seem to travel partly by way of the sympathetic system, partly by way of the autonomic system. From this it may be justly concluded that the entire vegetative nervous system is under the control of the glands of internal secretion.

Even if the proof of the existence of a hormone for the autonomic system ("autonomin") is not as yet conclusive, yet there is no doubt that there is some substance which exerts a continuous stimulating action upon the autonomic nervous system.^{4a}

⁴ Eppinger, Falta and Rudinger, *Zeits. f. klin. Med.*, Vol. 66, Parts 1 and 2, Vol. 67, parts 5 and 6.

^{4a} Translator's Note.—Acetyl-cholin is now regarded as the nearest approach to the "autonomin," since cholin exists in all body cells. Acetyl-cholin stimulates the autonomic throughout.

It is known that section of the sympathetic pupillary fibers will cause a persistent contraction (myosis), while section of the autonomic fibers will cause a dilatation (mydriasis). Similar results are obtained in many localities in the body where continuous impulses act upon smooth muscle, thus showing that there is a continuous stimulation of both of the antagonistic systems. Under normal conditions these two forces seem to be in equilibrium, a fact which serves to cut off their continuous activity, i. e., the activity of one or another never appears to its fullest extent. Such a continuous activity of nerve impulses on smooth muscle cells is termed *tonic innervation*.

The result of this is an averaging of these antagonistic forces which may approach now one, now the other extreme. In many organs, upon which both systems act, there is no distinct antagonistic musculature, as is true in the case of the pupil, but a single muscle only, and yet stimulation of one or the other system will cause contraction or paralysis. The same thing applies to glandular activity. The many possibilities which may occur in the realm of the two nervous systems will not be discussed. The fact that antagonistic actions may be obtained by stimulation of these two systems must suffice. The impulses arising in the antagonistic systems may vary greatly both in intensity and in duration. The resultant of the two antagonistic forces is a partial measure of the impulses coming from the two systems. These have been shown, by experiments upon animals, to have the greatest variations.

After a lasting stimulation proceeding from one of the two systems has occurred, a different type of equilibrium of the end organs results. From this it is seen that according to the intensity of the lasting nerve impulse, the temporarily varying stimuli which result from the mutual relations of the organs of the body and its food, may be translated, with varying degrees of ease, into mechanical or secretory activity. Thus under certain conditions small stimuli may cause large reactions, either physiological or pathological. This is so because only a little additional influence is needed to produce a noticeable irritation. Furthermore, it is to be expected that trivial and even transitory stimuli, which act upon an established condition of increased tonus, may produce prolonged and pronounced results. The antagonistic

systems play the very important rôle on the one hand of moderating physiological impulses which might reach very marked intensity, and on the other of preventing acute transitions from rest to excitation or vice versa. Their normal activity therefore subserves the purpose of preventing the functions of visceral organs from going rapidly from one extreme to the other.

It is quite possible that in the central nervous system there exists some common center which controls the antagonistic actions of these two systems. It is clear that a disturbance of the antagonistic control may cause a stronger or weaker irritability, or an increased or decreased tonus in one of the two systems, which may become the basis for the development of a pathological condition.

In the following pages it will be shown how much value this conception may have, not only in the field of general pathology, but also as an aid to the comprehension of various disease pictures. We shall also try to show whether many conditions which, owing to their symptomatology, are called "neuroses" may be not made clear in the light of what has just been said. For clinical reasons it seems best to study first the condition of tonus or irritability of the "autonomic" nervous system.

If at this point one compares the terms tonus and irritability at once it will be seen that they are not identical. Pharmacological experiments show that physostigmin, so far as its effects upon the heart go, only increases the irritability of the vagus and causes no appreciable results unless other stimuli enter. On the other hand muscarin acts as a primary stimulant and causes cardiac standstill without the intervention of other stimuli. Thus physostigmin increases the irritability while muscarin increases the tonus. At this point one must recall another drug, namely strychnin, which only increases tonus, and does not have a direct stimulating effect.

Next considering the observations of experimental physiology, it is found that for physiologists the idea of vagus tonus is an old one. It is well known that in the most varied kinds of animals stimulation of the vagus will cause great changes so far as the heart is concerned. Sometimes a mild stimulus will cause cardiac standstill, while in other cases the strongest induction current will not produce any effect upon the heart. These variations appear

even after bilateral vagotomy. Vagotomy itself will sometimes cause a marked tachycardia, while in other instances no influence of the vagus upon the heart rate can be noted. These variations are not only to be observed in different species of animals but even in animals of the same species. The vagi of young dogs and guinea pigs are said to possess great irritability, while those of adult dogs and rabbits possess a low irritability. The term employed to designate this large individual variation is high or low vagus tone. In general, this conception was only applied to the heart, since it is easy to see that much more difficulty attends measurement of the effect of the vagi upon other organs, and thus knowledge on this side of the subject was much less clear. The experimental methods are in part to blame for this, since narcosis and even curare may cause a great decrease in the irritability of the entire vagus.

Since the conception of vagus tone has been established in experimental physiology and in pharmacology it is not amiss to attempt to apply it to clinical problems. Many observations support the idea that there are individual and varying degrees of tonus of the vagus system in man. The variations in activity of vagotonic drugs afford examples. In many individuals, even small doses of atropin, which cut out already existing vagus impulses, produce marked tachycardia, dry mouth, fever, mydriasis, paralysis of the ciliary body, hallucinations, and sometimes glycosuria. In other individuals, the usual dose is practically without action. Similar variations occur with pilocarpin. One frequently hears physicians complain that many people do not sweat when pilocarpin is given. And other substances which act upon the vagal system, such as digitalis, morphin, scopolamin, hyosciamin, etc., have varying degrees of action in different individuals. These variations are regarded as idiosyncrasies, by analogy to the varying degrees of reactivity which individuals show to such drugs as iodine, cocaine, salicylic acid, etc. We may say at once that these as well as other clinical facts, such as respiratory arrhythmia, habitual bradycardia, etc., have furnished the means of drawing our attention to the variations in the tonus of the vagal system in man.

We have designated this type of individual "*Vagotonics*." Under the conception of vagotonia we include all those constitu-

tional conditions in which, in addition to the manifestations of a functionally increased vagus tonus and increased irritability in this anatomical system, there also exists a condition of increased sensitiveness to pilocarpin. In the light of the previously described antagonism between the two parts of the vegetative nervous system, we may add as a further earmark of the vagotonic disposition a relative decrease of reactivity to sympathetic stimuli.

Before proceeding further, two subjects must be considered which may baffle the recognition of or lead to errors in the diagnosis of the symptoms of vagotonia. These concern the vasomotor system and the automatism which exists to a certain degree in every organ.

Physiologically the significance of this automatism becomes clear when we see that all visceral organs have a definite automatism, even if all nerve impulses are excluded. It is difficult to decide whether the ganglionic impulses connected with these organs are the cause of this automatism, or whether the source of the activity lies within the muscle elements themselves.

The fact that of the various drugs, which have selective action upon the vegetative nerves, some have a paralyzing, some a stimulating action upon the isolated organs speaks in favor of the nervous theory.

The vasomotor system may be considered as occupying a special position since its main function is to react to the momentary demands for the balance of the blood supply of the entire body. Both the nutrition and the functional activity of certain organs require a plentiful blood supply which causes a reversed condition in other organs which are at rest at that time. Of course these changes depend in the end upon a normal play of vasodilators and of vasoconstrictors. Since these depend upon visceral nerve influences, the vasomotor distribution of blood depends upon a greater or smaller irritability of these nerves.

We believe that in cases in which the vascular reaction is reversed the stimuli which come from visceral nerves should be considered as playing the principle rôle. Later, we shall consider the fact that the distribution of the blood supply, either too much or too little, may disturb the function of normal visceral stimuli.

4. PHYSIOLOGICAL OBSERVATIONS

The question now arises: In which organs are we able to estimate the condition of tonus of the autonomic system, and what symptoms are significant of an increase of the tonus or of an increased irritability of this system, in the sense of the term "vago-tonia"? It will be necessary at this point to comment briefly upon the anatomic and physiologic relationships which exist between the extended vagus and the internal organs.

For clinical purposes it suffices to recall the following physiological facts. The autonomic system gives rise to that part of the oculomotor nerve which supplies the ciliary body, the pupil and in all probability the levator palpebrum. Stimulation of the autonomic nerves therefore causes contraction of the pupil, spasm of the ciliary body (accommodation spasm) and widening of the palpebral fissure, the last being due to increased tonus of the levator muscle. Another branch of the autonomic nervous system lies in the chorda tympani. This innervates the salivary glands. Another nerve which is functionally but not anatomically related to the chorda tympani is that of the lachrymal glands. Stimulation of these fibers, as by pilocarpin, will cause increase in the salivary as well as in the lachrymal secretions. At the same time the skin of the face and head becomes red, due to vasodilation, so that it may be assumed that (most probably) the vasodilators of the skin vessels of the head, including the mucous membrane, can also be stimulated by the autonomic nervous system. To what extent the erector muscles of the hair are governed by autonomic stimuli cannot be stated. All that is known is that sympathetic stimuli, as for example adrenalin, will produce "gooseflesh." In man it is most probable that the secretion of sweat is dominated by the autonomic (vagus) system, though up to the present time no anatomical or histological proof of this exists even in animals.

The vagus itself, in its narrower sense, innervates the heart, lungs and intestinal canal. It is as is well known the inhibitory nerve of the heart. The inhibitory influences act upon the rate of the beat of the heart (slowing of the pulse, or negative chronotropy), upon the strength of the contractions, diminishing the cardiac strength (negative inotropy), diminishing the threshold for stimuli which may reach the heart (negative bathmotropy).

Furthermore, vagal stimuli may diminish the transmitting power of the nodal system between auricle and ventricle (heart block or negative dromotropy). Finally, it is supposed that vagus stimuli diminish the tone of the heart muscle and thus increase the diastolic excursions (vagal action upon the diastole—Luciani).

From the clinical point of view there are only two actions of the cardiac branches of the vagus which merit consideration. These are: (1) Diminution of the rate of the heart beat; (2) diminution of the transmitting power of the nodal system.

The influence of the vagus upon the heart is lasting, but not always of uniform strength. This is best shown by considering respiratory changes. During inspiration the tone of the vagus is diminished; during expiration it returns to normal. The result is a respiratory arrhythmia which consists essentially in an inspiratory acceleration and an expiratory slowing of the heart beat (H. E. Hering).

Arterial pressure is only secondarily under the influence of vagal impulses. Peripheral vasodilation as well as slowing and weakening of the heart beat may cause a fall in blood pressure. But it must not be overlooked that vagotropic substances have a vasodilator action upon excised peripheral vessels in contrast to the dilating action of adrenalin (Langendorf) upon the coronary vessels.

As to the influence of the vagus upon the bronchial branches, we know that stimulation will cause contraction of its smooth musculature. Since the fibers which supply the musculature of the larynx (*n. recurrens*) also run with the vagus, we may say that this nerve also dominates the "rima glottidis." It may thus be considered in the clinical observations which follow. As regards the function of respiration, the respiratory center as well as the autonomic nervous system take a share, so that, by means of a kind of autointerruption, we have the vagus acting as an antagonist to the autonomy of the center. If the vagus endings in the lungs are stimulated by a deep breath inspiration is inhibited by way of the vagus and expiration is made possible.

In the sphere of the upper digestive tract, the vagus can influence not only the secretions but also the state of motility and contraction of the smooth muscle. It is known that autonomic stimuli increase the secretion of the gastric mucous membrane, the result being hypersecretion with or without hyperacidity.

Vagal stimulation may also cause turbulent gastric peristalsis, which may readily change into atypical (retrograde) peristalsis and may even manifest itself in vomiting. No doubt the occurrence of folding of the gastric musculature, which is caused by an increased tone in the stomach, is due to a similar action.

Since we know that the opening of the pylorus is dependent upon the degree of acidity of the stomach contents, we see that there must exist a relation between the activities of the pylorus and the tone of the vagus. That the cardiac musculature and the sphincter pylori are supplied by the autonomic, particularly in man, cannot be denied in the light of the good effect of atropin upon pylorospasm and cardiospasm. Furthermore, vagus stimulation causes spasm of both of these sphincter muscles.

Concerning the dependency of the motility of the esophagus upon the nervous system little is known experimentally. Irritation states of the esophageal musculature (esophagospasm) are relieved by drugs which paralyze the autonomic system. Coördination of the movements of swallowing, particularly of the progress of food from the mouth to the esophagus, is a function of the swallowing center which is activated by stimuli going from the posterior pharyngeal wall. The clinical significance of this fact will be considered later.

The mechanism of the intestinal movements is hidden in uncertainty. Its activity is regulated not only by the vagus, and the splanchnic nerves of the sympathetic system, but also by the automatically acting plexi of Auerbach and Meissner. Hence certain drugs, such as ergot and the substances of the digitalis series (Magnus), may produce motor activities by direct action upon the intestinal musculature without interference of the nervous apparatus. If one stimulates the motor vagus endings in the intestine by pilocarpin, or physostygmmin, the activity of the rolling movements of the intestines, particularly of the small intestine, is increased and in this manner the emptying of the contents accelerated. Under other conditions, however, a tonic spasm of the sphincters may result from the existence of too much tonus, and a spastic condition of the gut will result. The opposite effect is observed following the administration of atropin, which paralyzes the vagus and depresses and quiets the intestine. It is readily seen, therefore, that the action of atropin will be best observed in such instances in which an increased tonus of the

vagus, or vagotonia, has led to an abnormally increased tonic peristalsis. If, on the other hand, the tone of the vagus is low (atony of the intestines) cutting its influence off by atropin is of little avail. In view of the fact that atropin stimulates the ganglion cells of Auerbach's plexus, it may, in case of atony, cause the strengthening and slowing of peristalsis. Finally, it is of significance to clinicians to know that pilocarpin, in animals at least, may increase the secretions of the lower intestinal segments.

Autonomic stimuli cause spasm of the smooth muscles of the gall bladder and of the pancreatic duct. The influence of the nervous system upon the secretions of the liver and those of the mucous membrane of the gall bladder is not known with certainty, but pilocarpin increases pancreatic action, in contrast to the action of atropin and adrenalin.

The lower segments of the intestines (the descending colon, sigmoid and rectum), as well as the bladder and genital organs, receive their autonomic stimuli through a special nerve, the pelvic. Stimulation of this nerve evokes spasm of the sphincter ani, contraction of the detrusor of the bladder and simultaneous opening of the sphincter vesicæ and erection of the penis.

A few words remain to be said regarding the connection of the autonomic system with the blood and with metabolism (Stefani). Pilocarpin, a vagotropic substance, causes eosinophilia (Neusser⁵) while atropin and pilocarpin cause this to disappear.⁶ It is also an established fact that pilocarpin can arrest adrenalin glycosuria.

Inasmuch as experiments upon the influence of the vagus upon metabolism have been carried out almost exclusively upon lower animals, it is difficult to attempt an account of its action. There is, however, no doubt that owing to its close relations to the glands of internal secretion, the autonomic nervous system has a marked influence not only upon the pancreas and thyroid glands, but also upon the entire mechanism of metabolism.

Although in the first chapter brief mention was made of the fact that all the bodily organs are doubly innervated, *i. e.*, have a nerve supply from each of the antagonistic systems, the auto-

⁵ Neusser, E., Hämätologische Studien, Wiener klin. Wochenschrift, 1893, Nos. 3 and 4.

⁶ Bertelli, Falta, u. Schweeger, Über Chemotaxis (Wechselwirkung der Drüsen mit innerer Sekretion, 3 Mitteilung), Zeitschrift f. klin. Medizin, 1901, Vol. 71, Hft. 1 and 2.

nomic and the sympathetic, it must be emphasized again that though as yet only one of these antagonists has been considered, there still remains the fact that every visceral organ is supplied by sympathetic fibers, which work antagonistically to the autonomic supply.

Hence it may be stated that the normal progress of functioning of visceral organs is a well regulated interaction between two contrary acting forces. Too much activity on the part of one, or too little on the part of the other will result either in motor or secretory inhibition or stimulation and may bring about a condition of disease. Since this plus or minus condition is to be seen as the expression of an increase or decrease of tone, the degree of difference between the state of equilibrium and the extremes of stimulation in one direction or another, autonomic or sympathetic, serves as an index of the state of tone in one or the other of these symptoms. It appears to be possible for variations from the normal equilibrium to exist without causing disease.

5. DIAGNOSIS OF VAGOTONIA IN MAN

In the course of investigating the varied reactivity of different patients to pilocarpin hydrochloride (0.01 gm. by hypodermic) it has been found that those who react with sweating and salivation also show other symptoms which in all probability point to an increased tonicity of the autonomic. Often normal individuals, who on the basis of an overreactivity to pilocarpin were suspected to be vagotonic, unexpectedly showed, on more careful search, such symptoms as hyperacidity, eosinophilia, bradycardia, mild arrhythmias, particularly respiratory, or sluggish bowel action, approaching spastic constipation, all of which were borne by the patient without comment, the only complaint being sweating and salivation.

Whenever pathological conditions, which could readily be interpreted as the result of autonomic stimulation existed, the susceptibility to pilocarpin was found to be very great. Among these patients are such as seek the physician's aid for troublesome salivation, pylorospasm, the discomforts of hyperacidity, bronchial asthma, spastic constipation, gall stone colic, gastric crises, etc. Furthermore, latent pathological disturbances were frequently made more acute by an injection of pilocarpin. In a case of beginning *tabes dorsalis* a mild form of crisis resulted from

an injection of pilocarpin; in another case a typical attack of bronchial asthma was provoked by an injection. Later on it was discovered that similar instances had occurred, the significance of which had not been appreciated. Furthermore, it is to be observed that pilocarpin may increase the various symptoms just spoken of to such a degree as to cause considerable discomfort, such as a feeling of pressure in the gastric region, combined with the continued pains due to hyperacidity, states of anxiety in vasomotor angina pectoris, etc. The fact that atropin exerts a beneficial effect upon most of the symptoms which have been described is a further proof that most of them are ascribable to autonomic stimuli.

These symptoms show that in individuals who are hypersusceptible to pilocarpin there are evidences of a condition of increased tone in the entire autonomic system. Furthermore, they point the way by which other manifestations of spontaneous increase in irritability or tonus in other parts of the autonomic systems may be recognized, since it seems probable that the condition of increased vagus tone is not solely local, but exists throughout the entire autonomic system. As a matter of fact, many instances of increased tonus or conditions of spasm were found in regions which previously have not been heeded.

In the following paragraphs, those symptoms occurring in man which are indicative of a departure from the normal will be considered in the same order as in the section on physiology.

EYE: The tension of the zone of Zinn or stimulation of the ciliary muscles, evoked by activity in the autonomic system, causes an increase in the sphericity of the lens.

If the ciliary muscle goes into a state of spasticity the near point of the eye will become nearer, due to increased curving of the lens. The accommodation spasm which is seen in young people as the result of steady work with objects placed close to the eyes may be increased—possibly discovered—by the use of pilocarpin, and may be relieved by atropin. Aside from spasm, we may say that the tonus is increased when the paralyzing action of atropin is but transitory, and that the strong autonomic tonus soon overcomes the paralysis due to atropin. This state of affairs which is very frequently observed in young individuals with accommodation spasm is closely related to that condition in old people in which the action of atropin is a very lasting one, because

the tonus remaining in the ciliary body is but small. Thus the visible effect upon the width of the pupil cannot be great, since omission of the already small amount of tonus cannot cause a difference of great degree. By analogy, similar differences may be expected from the use of pilocarpin and cocain. The paresis of accommodation during convalescence from various severe diseases, as for example diphtheria, must be mentioned at this point. When one considers that pilocarpin is used as a curative substance under such circumstances and has beneficial results, one is justified in believing that the result is due to a diminution of tone in the autonomic nervous system.

The Löwi phenomenon⁷ might be expected to be positive in just such cases. It is well known that in the normal eye adrenalin cannot overcome the permanent tonus of the sphincter pupillæ or of the muscles of accommodation. Only when the tonus of the sympathetic is increased generally, as for example in de-pancreatized dogs, can adrenalin, acting as a stimulant of the sympathetic nerve to the dilator pupillæ, have its full mydriatic action. In man as well one may find this mydriatic action. Löwi himself described this action in several cases of Basedow's disease and of diabetes. If on the contrary autonomic spasm existed, the pupil was myotic. That the state of excitability of the autonomic part of the oculomotor nerve may be influenced from afar may be observed from the fact that when there is a rise in tonus in other parts of the autonomic system, there is an overflow of energy which manifests itself in constriction of the pupil. An example of this was seen in cases of bronchial asthma or gastric crises. In connection with the latter, Freidreich has observed that an acute myosis is almost a typical symptom of gastric crises. Just as atropin has an inconstant action upon the ciliary body, so it may have the same upon the pupil. It is well known, furthermore, that in old people it is very hard to obtain an atropin mydriasis.

It has already been stated that pilocarpin—an exclusively vagotropic drug—as well as adrenalin, a correspondingly exclusive sympathetic stimulating drug, have found their clinical usefulness. On account of strongly differentiated action they have suggested the occurrence of individual variation in reactivity or over reactivity. Other interpretations are also possible on the

⁷ Löwi, Arch. f. exp. Pathol. u. Pharm., Vol. 59, p. 330.

basis of the here mentioned facts, all based upon experimental observations. Should not variations in tonus, in terms of reactivity of one or the other vegetative nervous system, throw some light upon clinical observations? It was to be expected that adrenalin would be particularly active in those in whom an increased sympathetic tonus or increased reactivity of the sympathetic existed, and on the other hand it was to be expected that pilocarpin would evoke an increased reaction in those substances in which the autonomic system was in a state of increased irritability.

We have already observed that an increase of tonus in one system almost rules out an increase of tonus in the other. [Note will be taken of the exceptions to these rules found in many nervous and mental diseases in another place.] If our contention is correct, that the reactivity of individuals to pilocarpin or adrenalin is exclusively dependent upon the tonus of the system affected, then there must be a pharmacodynamic antagonism. Individuals who are very reactive to adrenalin will be less reactive to pilocarpin, and strong pilocarpin reactions would imply reduced adrenalin reactions. Numerous investigations have proved this to be the case, and have made it very probable that there exists in man as well a pharmacological antagonism between pilocarpin and adrenalin. In this fact, based on a large mass of clinical material, we see a new stimulus for the opinion that the tonus of the visceral nervous system, or more properly speaking of its endings, must play a rôle in clinical medicine.⁸

It now becomes a question whether or not pilocarpin [or adrenalin], may produce in susceptible individuals clinical as well as pharmacological manifestations which would differentiate the two antagonistic systems. The fact that individuals who are over active to pilocarpin may be observed to have a latent condition of vagotonia in the sphere of the autonomic system which may take on the characteristics of disease symptoms, leads us to conclude that it is not improbable that an increase of tone of the autonomic system may exist not only in such localities where pilocarpin acts, but also in all parts of the autonomic system.

The levator palpebrarum also is most probably innervated by a branch of the autonomic nervous system. Its behavior under the influence of certain drugs speaks greatly in favor of the belief.

⁸ Eppinger u. Hess, *Zeit. f. kl. Med.*, 67, 5 u. 6; 68, 3, 4.

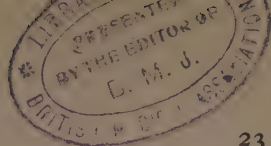
Pilocarpin instilled into the eye will cause widening of the palpebral fissure. In suitable cases, a condition much like the presence of a v. Graefe's sign may be noticed so that we can have no hesitation in attributing this symptom to an increase of tonus in the levator muscle. In many cases of vagotonia widening of the palpebral fissure may be observed, an additional fact impelling us to believe that it is a symptom referable to increased autonomic tonus.

Moebius' sign, a condition in which the eye-balls do not converge on near fixation, seems to be due to stimulation opposite to that which would be produced by increased autonomic tone. It is difficult to explain this, but the question arises whether, since the oculomotor nerve carries autonomic fibers, it might not, in controlling the mechanism of convergence, be subject to the same variations in tone as it is in controlling other mechanisms.

It is notable that in vagotonic individuals a mild spasm of convergence, a kind of convergent strabismus, has not infrequently been observed. Exophthalmus is to be regarded as the result of a stimulus opposed to the autonomic system, since it is caused by spasm of a muscle whose innervation is derived from the sympathetic nervous system. Finally, it may be added that epiphora was frequently observed among vagotonics.

SALIVARY GLANDS.—Salivation is the result of a state of autonomic stimulation of the salivary glands. Atropin can readily relieve this condition. Increased salivation is a not infrequent occurrence in cases of nervous people whom we have designated as vagotonics, and from the beginning of this investigation, the occurrence of increased salivation after pilocarpin was found to be typical of vagotonics. Further, when the vagus was extremely irritable, not only did salivation result from the administration of pilocarpin, but also increased secretions from the nose and eyes. In certain tabetic crises, which were plainly of autonomic type, salivation was occasionally observed. The typical vagotonic never has a dry mouth.

SKIN.—Sweating after administration of pilocarpin [or physostigmin] is considered a symptom of vagotonia. A sign of increased autonomic tonus corresponding to this is the tendency to sweat of which so many people complain, and which so often assumes pathological proportions. Vagotonics, in reacting to cer-



tain stimuli, are subject to an exaggeration of the normal mild transpiration, namely, actual sweating.

Attacks of sweating are associated with many other conditions of increased tonus in other parts of the vagus, such as nausea, vomiting, asthma, angina pectoris, gastric crises and so forth. In some people only circumscribed areas of skin are involved, as the hands, feet, head, back or thorax.

Many infections are complicated at their crisis by sweating. The concomitant bradycardia adds proof to the supposition that here also there is something which stimulates the autonomic nerves of the skin and heart. A frequently observed symptom, for which no theoretical explanation could formerly be given, is that vagotonics have moist hands and feet, and that these extremities are usually of a livid color, which becomes dark purple in winter, and can readily be blanched by pressure. Such people usually complain of having cold hands and feet continually. This must necessarily be regarded as a deviation from the normal distribution of blood. In many instances, a weight upon the abdomen, as for instance a sandbag, had a very beneficial effect upon this condition of the hands and feet. Of course we have to deal here with a vasomotor disturbance, but it is difficult to explain since it is just the relations of the vasodilators and vasoconstrictors to the visceral nerves, which are but little understood. However, this much may be accepted: Autonomic drugs stimulate the peripheral vasodilators in contrast to adrenalin which stimulates the peripheral vasoconstrictors. A proof of this is that pilocarpin causes reddening of the face as well as of other parts of the body. X

This leads us to the consideration of another phenomenon, namely dermatographism. This may be divided into two types; one the dilator type, which is characterized by reddening, swelling and even exudation, following stimulation of the skin, the other, the constrictor type, characterized by pallor of the skin where it has been irritated by a firm stroke of the finger. These observations have their exception since skin which is sweating profusely will show no signs of dermatographism. Gooseflesh, which is due to a stimulation of the sympathetic supply to the erectores pilorum, is rarely seen among vagotonics.

In concluding the observations upon the changes seen in the skin, a few words will be said in regard to its pigment. Pig-

mentary changes are seen in the most varied pathological conditions, such as pregnancy, Addison's disease, Graves' disease, vitiligo, naevi and so forth. In Addison's disease, particularly, these changes are very prominent. The latest experiments concerning disturbances in post mortem pigment production in adrenalectomized dogs, and the absence of these disturbances when adrenalin has been administered, speak strongly in favor of a relation between pigmentation and autonomic stimuli [Konigstein].⁹

Frogs' skins also are controlled by the autonomic system, as the mechanism of production of pigment in them proves. When adrenalin is injected there is almost a complete disappearance of pigment. Increased production of pigment is found not only in Addison's disease, but also in a number of other nervous diseases [Graves' disease] in which the presence of increased autonomic stimulation may be assumed. (Tr. Note: Due rather to absence of sympathetic or adrenal activity than to the presence of autonomic stimuli.)

HEART.—That type of bradycardia which changes into tachycardia under the influence of atropin must be considered as a typical manifestation of increased vagus tone.¹⁰ As an example of this type of bradycardia we may take that occurring in icterus due to stasis of bile in which retained salts of bile acids affect either the central or peripheral endings of the vagus. In young people in particular, a bradycardia is a certain sign of vagal stimulation.

H. E. Hering¹¹ has stated recently that the failure of a reaction after the normal dose of .001 gr. of atropin [subcutaneous] does not signify with finality the absence of increased vagus tone, since higher doses could produce tachycardia and pressure upon the vagus nerve showed that the inhibitory nerves were irritable. We can confirm these observations and can add that in particularly obstinate cases the opposite is often to be seen, namely, the frequent action of atropin in producing not tachycardia but bradycardia.

This may perhaps be explicable by supposing that after a mild inhibition of the autonomic system by small doses of the drug there ensues a marked increase in vagus tone, causing a bradycardia.

⁹ Königstein, H., Über postmortale Pigmentbildung. Münch. med. Woch., 1909, No. 45.

¹⁰ Dehio, Deut. Arch. f. kl. Med., 52, p. 97.

¹¹ Hering, H. E., Münch. med. Woch., 1910, No. 37.

Atropin can always obliterate the bradycardias resultant upon certain acute infections, as for instance in diphtheria, or in the convalescent stage of febrile angina, mild pneumonia, typhoid, erysipelas, acute articular rheumatism, and scarlet fever. This action implies that the bradycardia is the result of increased tone in the vagus. If this reaction to atropin fails it may be assumed that organic changes exist. The type of bradycardia which is best and longest known is that accompanying increased intracranial pressure, as in cases of brain tumor, hydrocephalus, pseudo-tumor of the brain, hematoma of the dura mater, and incipient meningitis. These bradycardias are always referable to cerebral stimulation of the vagus. In these cases there is also an individual variation so that certain cases may be instances of latent vagotonia. The effects of the increase of intracranial pressure are well shown by the administration of adrenalin. After an injection of this drug which contracts peripheral vessels but has no apparent effect upon the cerebral vessels, there occurs a flow of blood to the brain followed by an increase of intracranial pressure. This stimulates the vagus center, and causes a pulse characteristic of increased vagal action which may be relieved by atropin or vagotomy. Many drugs acting upon the heart can cause a bradycardia through vagal stimulation. Thus, after very small doses of digitalis its bradycardiac action may be so prominent that its entire cardiac action cannot be obtained without simultaneous administration of atropin. This bradycardia from digitalis is usually associated with other symptoms of autonomic stimulation, as for example digestive disturbances and vomiting. Similar idiosyncrasies must be considered if the various results of physostigmin in paroxysmal tachycardia are to be explained. Pilocarpin can hardly be included among the stimulants of the chronotropic functions of the vagus nerve.



Vagotonics often give evidence of a great deal of cardiac activity when the precordium is inspected. Closer investigation of this heaving shows that it is not accompanied by increased cardiac action, as occurs in valvular disease, but, as the X-ray examination shows, that there are great variations in the size of the heart in systole and diastole. This symptom is frequent in vagotonia, very frequent in the vagotonic type of Graves' disease [Basedow-thymus], and in the so-called goiter heart [F. Kraus].

In vagotonic bradycardia, the stimulus acts at the sino-auri-

cular node, but it may also act in the region between the auricle and ventricle. The result of this latter is that not every auricular contraction finds its way into the ventricle, and that the auricle beats oftener than the ventricle without any incoördination between the actions of the auricle and ventricle. The characteristic of "nervous" heart block [omitted ventricular systole of Hering] is that it may be relieved by atropin. The same result may be accomplished by adrenalin. But those bradycardias which are the result of disease of the heart muscle may be bettered by atropin through its beneficial action upon the transmission of impulses of the nodal system, and may show a slight increase of the pulse rate. Now and then, the "block" may involve but part of the nodal system, and may show transitorily those types which are demonstrated electrocardiographically when there is disease in one or another part of the nodes of Tawara.

An officer, aged 50, has complained for one year of occasional feelings of pressure in the region of the heart, with pains passing outward into the left arm. During all of these attacks, which have become more frequent of late, the patient has sweated profusely, and has vomited in some of them as well. He has observed himself with care, and states that during the attacks his pulse goes from 88 to 50-56. The patient gave a history of lues. He does not seem old. His face is somewhat red, and he perspires readily. Blood pressure varies from 120 to 180. The second aortic sound is accentuated. The heart itself is not enlarged. Since the electrocardiographic examination of the patient interested us most, other details will be but superficially considered. During a period when the patient was in normal condition [pulse 86], the electrocardiogram was of normal character. In all the three leads, there was a positive R wave, and positive subsequent wave. During an attack in which he experienced the above described feelings of depression—pulse 54—the following was found: The auricular wave remained at the same distance from the R wave. The R wave, which was small before, was now three times as wide. Furthermore, it was noted that at this time the subsequent wave was negative and came directly from the R wave. With the second and third leads, the R wave was negative and the subsequent wave positive. This condition was observed for some length of time [one hour]. It seemed of great interest to us to note that a subcutaneous administration of .001 gram of atropin relieved the bradycardia and at the same time changed the electrocardiogram to what it was before. There was no gallop rhythm during the bradycardia.

Of course all heart diseases cannot be diagnosed in this manner even if atropin does relieve them. There are cases which owe their disturbance to auricular or ventricular extrasystoles. To what degree this condition may be correlated to the physiologic fact that the vagus is a negative inotropic nerve is hard to say.

Some physiologists deny that the vagus has an influence upon the caliber of the coronary vessels. Counterbalanced to this view is the fact that adrenalin dilates the coronary vessels not

only when excised, but when in situ in the beating heart [Langendorf and O. B. Meyer]. On the other hand, one is inclined on chemical grounds to believe that the influence of the autonomic system upon the coronary vessels plays a large rôle. It is an accepted fact that the vagus can cause spasm of the coronary vessel musculature, and may thus cause narrowing of the blood vessels. According to our experience, vasodilator drugs are often of great benefit in the condition of angina pectoris. Nor do we presume too much in stating that many cases of angina pectoris, particularly of the vasomotor type, are referable to a condition of over-irritability in the autonomic nervous system. We would call attention to the good effect of vagoparalytic drugs, as well as to the fact that pilocarpin injections occasionally cause symptoms which resemble very closely the clinical picture of angina pectoris.

The cardiac vagus may be influenced reflexly as well as directly. The phenomenon longest known is that of Tschermak which is due to pressure upon the vagus nerve trunk. If one exerts pressure upon the vagus trunk in its course along the carotid artery in the neck region, certain individuals will react by a marked slowing of the pulse. The variations in this affect are great in various individuals and bear a close relation to the irritability of the vagus. Indirectly the vagus may also be stimulated through the trigeminal nerve. Some of the stimuli acting upon the trigeminus may be mechanical, as pressure on its branches, or faradic stimulation, while some may be chemical, such as tobacco smoke, chloroform or ammonia. These stimuli may travel by reflex paths to the vagus nerve and may cause bradycardia. Not only may the vagus branches to the heart be affected but others as well, as for example those involved in producing nasal asthma. A type of this reaction is without doubt the phenomenon of Aschner,¹² which consists of a bradycardia dependent upon pressure upon the eyeball. Since the eyeball is supplied by sensory branches of the trigeminus, this reaction is of the same kind as that due to stimulation of the nasal mucous membrane, which we know to be innervated by the trigeminus. Aschner's phenomenon has been found to be a most frequent occurrence in vagotonics, and, moreover, it may be readily eliminated by the administration of atropin.

Of interest in connection with the foregoing statements are

¹² Aschner, B., *Wien. klin. Woch.*, 1908, No. 44.

some experiments of R. H. Kahn. He was able to show electrocardiographically that adrenalin will produce changes which may be obtained to some degree by experimental stimulation of the vagus. He noted lengthening of diastole, blocking of impulse transmission, and automatic as well as weakened ventricular beats. But of greatest interest are his findings of a long series of dissociated auricular and ventricular beats. After he had been able to show that bilateral vagotomy eliminated all of these changes, he came to the conclusion that they were due to a rise in blood pressure in the brain, causing a stimulation of the vagus center. Clinically, we have observed that in some cases of vagotonia adrenalin injections produced cardiac arrhythmia without any con-comitant glycosuria. These we believe to be similar manifestations to those found by Kahn in animals, after adrenalin injections. We shall go into the details of this matter at another time. At any rate it seemed exceedingly significant that these cardiac arrhythmias only occurred in those who showed some other evidence of increased autonomic irritability.

LUNGS AND RESPIRATION.—The classical example of vagus stimulation in man is bronchial asthma. This, according to the prevailing opinions, is due to a spasm of the bronchial musculature. A substantial support of this view is the beneficial effect which atropin and adrenalin have upon the condition. The production of the symptoms of bronchial asthma may be explained as follows: Due to an over-irritable state of the vagus, even small stimuli acting upon it may produce spasm of the bronchial musculature. The result of this is that the alveolar air cannot be forced out as readily as normally by the elastic fibers and the condition of "passive" spasm, with the result that an excess of air remains in the alveoli. Furthermore the autonomic stimulus produces not only muscular spasm, but also increased secretion from the bronchial mucous membrane, an added hindrance to expiration. An argument in favor of this conception of the part played by the vagus is the action of adrenalin. This diminishes the bronchial secretion with the result that the spasm seems to pass away.

It is more difficult to understand a condition of increased vagal tone in connection with the lungs. However the following experiment may be taken as an example of the existence of such a condition. If an individual breathes in a Bohr respiratory appar-

atus, the following may frequently be observed. After a deep inspiration and a deep expiration have been taken and after the patient has again resumed quiet respiration, the curve does not drop to the previous level at once but with a slow and step-like fall (Fig. 2).

Individual variations play a part in this, as Hofhauer has pointed out, and these variations are due mainly to the expiratory muscles [the abdominal press]. It is noteworthy that after atropin the curve sinks much more precipitously, and there is no step-like formation. This, we believe, is to be explained by an increased tone in the vagal branches of the lung, causing narrowing of the bronchial musculature, so that an excess of air in the

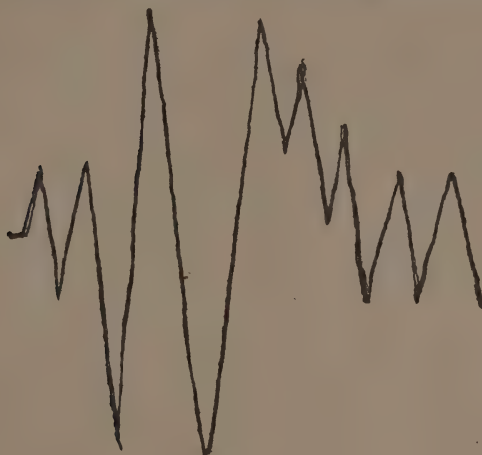


FIG. 2.

alveoli cannot be so readily expressed through the elastic elements of the lung. Later, this condition will be considered in connection with the occurrence of juvenile emphysema.

Strümpell's¹³ observation that narrowing of the glottis may occasionally complicate asthmatic attacks is of importance in connection with our observations upon the relation of bronchial asthma to vagotonia. It seems particularly significant when one considers that the recurrent laryngeal nerve is a branch of the vagus. This leads to the question whether or not spasm of the glottis [laryngospasm] may not be a result of some irritability of

¹³ Med. Klinik, 1910.

the tone of the rima glottidis. We have noted elsewhere the significance of laryngeal crises as states of autonomic irritability. In this connection it may be added that the dependence of laryngeal crises upon an increased tone in the musculature of the vocal cords is made clearer by the observation that in tabetics, who have a tendency to laryngeal crises, simple movement of the laryngeal passages may suffice to bring on an attack.

A frequently observed condition in vagotonics is respiratory arrhythmia. Patients often complain of a feeling of inability to expire. If tracings of the respiration of such individuals are made by a Hofbauer pneumograph, variations in respiration of varying duration will be found. In this way one may discover disturbances of respiratory rhythm which cannot be detected by mere inspection or even by closer study.

The variations manifest themselves graphically as incomplete expirations and inspirations following closely one upon another, so that the respiratory curve sometimes falls, sometimes rises. The respiration may also show pauses of varying duration. But one must take care not to confuse these arrhythmias with those produced by swallowing movements. Atropin will eliminate these irregularities, while pilocarpin will either bring them to light or aggravate them. We have noted beautiful examples of these arrhythmias during tabetic crises and in cases of vagotonic Graves' disease.

The relations between respiration and circulation may also show variations from the normal in vagotonics. There are definite variations in blood pressure and cardiac action dependent upon expiration and inspiration. In young people these variations may be considered to be normal. They consist in an acceleration of the pulse rate during forced inspiration which changes to slowing at the height of inspiration. Without entering into a discussion of the etiology of this phenomenon, we may say that it is eliminated by the use of atropin. This form of irregularity is designated *pulsus irregularis respiratorius* and, as has been stated, is particularly frequent up to the age of fifteen. When it occurs after this age and is to any degree marked it must be considered as a symptom of vagotonia. The infantile type of pulse, in Mackenzie's sense, is similar. It consists of shallow pulsations followed by deep excursions, that is, the individual attacks are of unlike intensity. Respiratory variations from the

normal may occur with this. As in *pulsus irregularis respiratorius*, atropin will relieve the arrhythmical condition.

STOMACH.—The influence of the vagus upon the stomach may be considered in three parts: the influence upon tone, peristalsis and secretion.

The newer experiments [A. Müller] have shown that the tone of the stomach is dependent upon the substances which enter the stomach at the same time that food enters. The stomach normally is not dilated, but dilates actively in proportion to the degree of filling, thus causing the muscular elements to cover the contents closely. Tone is therefore a resistance to filling. This resistance may be increased by the activity of the vagus, or by drugs which have a stimulating influence upon the autonomic system. While the atonic stomach reacts very readily upon ingestion of food, this same food must contend with a great deal of resistance in the hypertonic organ, a resistance which disappears but gradually. The progress of this disappearance may be

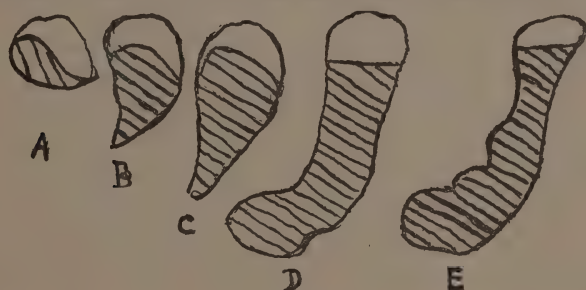


FIG. 3.

followed very satisfactorily in man by means of X-ray examinations. Bräuning¹⁴ was the first to show that the bismuth meal does not sink at once along the lesser curvature of the stomach to the antrum pylori, but is held back for varying lengths of time in the fundal parts of the stomach [see Fig. 3]. In some people it may be seen that the food is gradually forced out of the fundus, this part taking the form of a narrow canal which is but gradually expanded. The whole process would seem to be an economizing of space. If more food comes down through the esophagus, the fundal part fills up to a greater degree, then the pars intermedia is gradually distended, and finally the bismuth is seen to have

¹⁴ Bräuning, Münch. med. Woch., 1909, 20.

passed into the antrum pylori. In most instances a powerful wave of peristalsis is set up in the pyloric region when the food enters it. If the entire stomach is filled, as just described, a process which often takes several minutes, the form of that organ is called the "cow-horn" form, as described by Holzknecht. This gradual filling of the stomach may occur in quite normal individuals who complain of no stomach trouble whatsoever. Should the resistance of the stomach musculature be lacking, its tone will play but a small rôle, and the food will fall directly into the lower pole of the stomach which under these circumstances will be "hook-shaped," a term also introduced by Holzknecht. It is very significant that the first form of filling of the stomach, that leading to the "cow-horn" shape, is most frequently seen in vagotonic individuals, so that we may suggest for it the designation *vagotonic form of stomach*. Mention must be made at this point that Holzknecht has stated that this form of stomach is more frequently found in young individuals than in adults. It is certainly striking to find the vagotonic form of stomach occurs in individuals with flabby abdominal walls in whom one would expect ptosed and atonic stomachs. This occurs chiefly in women who have borne children frequently and in whom the supporting apparatus for the stomach tone is lacking, for when the abdominal pressure is decreased there is almost always a decrease in the tone of the stomach. If under such circumstances a vagotonic form of stomach is found, the probability of increased vagotonia is all the greater.

It is known that gastric peristalsis is increased by pilocarpin and physostigmin, while small doses of atropin inhibit it. Furthermore, a physiologically increased peristalsis would indicate an increased tone of the autonomic system. But it must be stated that increased tone and increased peristalsis do not always go hand in hand, since there are stomachs with but little tone in which a powerful peristaltic action may be observed.

Hypersecretion as well as hyperacidity are traceable to stimulation of the vagal nerves of the stomach. Here it becomes necessary to differentiate between latent increased tonus and paroxysmal increase of the secretory activities. If we find in a vagotonic person very marked hyper-acidity, reaching double the normal, and find that in spite of this the person makes no complaint, it is justifiable to conclude that this increased produc-

tion of juice is dependent upon increased tone, upon some physiological stimulus. If the increased production of juice is accompanied by attacks of pain, we have the well-known picture of intermittent gastric secretion, a disease whose nervous etiology is generally recognized. There are many forms of increased glandular activity since hyperacidity and hypersecretion may be found together, or either one may be found alone.

The highest grade of apparently lasting stimulation of the gastric vagus is gastrosuccorhea [Reichmann's Disease], in which the tone, one might almost say the spasm, may reach such high limits that the usual doses of atropin have no effect. Pylorospasm is most often accompanied by hyperacidity. The spasm of the circular pyloric musculature, which is the underlying cause of pylorospasm, may reach so great a degree that not only is the passage of food into the duodenum made very difficult, but even waves of antiperistalsis may occur. This fact, which may be confirmed by X-ray examination, is important since antiperistalsis is so generally referred to some organic disease in or about the pylorus. As a means of differentiation, atropin may be tried, since this will check the pylorospasm as well as the antiperistalsis—clinically pyloric stenosis may be *caused* by spasm of the sphincter pylori. When these stomachs are examined radiographically, the previously mentioned physiological picture of increased folding of the gastric musculature is so much intensified that one may get a condition like that of the hour glass stomach dependent upon organic changes. Here also atropin may be used to advantage.

It is as difficult to explain cardio and esophagospasm as it is to say anything very definite about the physiology of the cardiac and esophageal musculature. Both conditions are typical diseases of vagotonics. Both may come on paroxysmally and are to be attributed to a periodic increase in tone. They are often relieved by atropin, though this is not always the case, a fact which seems to point rather to too small a dose of atropin having been given than to a belief that the condition is not due to vagal stimuli. Occasionally one is under the impression that atropin aggravates the condition, having an action contrary to its usual type, a phenomenon which we shall have cause to mention in other connections. We shall consider the possibility of explaining this anomalous action in the section on therapy.

A not infrequent complaint of vagotonics is that on swallowing food it seems to stick in the esophagus behind the heart. If one follows the progress down the esophagus of a mass of bismuth, great variations in the speed of passage may be seen. In not a few cases of typical vagotonics, one finds that the food passes slowly down the esophagus and even piles up, remaining stationary a short time. The assumption that the tone of the esophagus is decreased in many cases is rendered very probable by these findings. Here we must state that vagotonics have an almost entirely anesthetic pharynx, a phenomenon that will be more fully discussed later. Since cocainization of the pharynx or the places sensitive to the swallowing impulse may disturb the act of swallowing and also the passage of material down the esophagus, we believe that a similar condition exists in vagotonics, i. e., anesthesia of the pharynx with resultant disturbed swallowing and passage of food. In other instances, the bismuth meal is retained for a relatively long time in the esophagus, but it is found that this, instead of being dilated, is much constricted. It is just in these cases in which one sees very active gastric peristalsis and even antiperistalsis. One may also distinguish in the esophagus as in the stomach the difference between tonus and increased peristalsis.

Vomiting as it occurs in hysteria, in the early stages of pregnancy combined with ptyalism and further when cerebral pressure is raised due to some organic cerebral disease, is probably due to stimulation of the gastric vagus. At any rate experimental stimulation of the central end of the vagus will evoke vomiting movements.

THE INTESTINE.—In studying the nervous disturbances of the intestinal canal, we must first differentiate between the small and the large intestines. Functional tests of the jejunum and ileum are very difficult, since their motility may only be followed radiologically, and their secretory and absorption activity is to a great degree complicated by the compensatory action of the colon.

Autonomic stimuli cause an increase of peristaltic action in the small intestine. To determine the degree of this increase is difficult, the only certain criterion being the time required for a bismuth meal to pass from the stomach to the colon. In many vagotonics, this time is considerably shortened.

The mechanism of the musculature of the colon is very com-

plicated. The activities, much like the pendulum activities of the small intestine, appear to be very sluggish, and, if the newer investigations of Holzkecht¹⁵ be correct, are only periodic. It is far easier to determine the changes in diameter of the colon radiologically. If the colon contain a bismuth meal, many types are seen. In some cases, the ascending colon remains filled for a considerable time, which, due to the overtaking of its capacity, increases its diameter; while the transverse and descending colon are empty for a considerably longer period than is normal. In other cases, on the contrary, the ascending colon empties itself rapidly, while the transverse and descending parts contain the bismuth for a correspondingly longer period. It seems characteristic of this latter type of case that, as far as may be determined by the X-ray, the haustra appear to be very clearly defined. But in these cases also it may be seen that small parts of the bismuth which make up the fecal column are cut off and the entire lumen is narrowed. If the bismuth remains for a longer time in the descending colon, it may conform to the first described type and remain in this location the longest time. Finally there is another frequently observed type in which almost the entire colon is free of bismuth, and almost all of the bismuth is piled up in the sigmoid or ampulla.

Without having any *a priori* opinion, we can state that we have noted both diarrhea and constipation in our cases of vagotonia. To explain the diarrheas is not at all difficult from the point of view of vagotonia, since it is known that pilocarpin will cause this condition in animals. In these cases both increase of peristalsis and increased serous transudation in the intestinal lumen play a part. As a matter of fact, diarrheas are found in various conditions of increased irritability of the vagus, as in Addison's disease and the vagotonic types of Graves' disease. They may be produced by pilocarpin, relieved by atropin, if the individual be at all predisposed to them, and it may be added that adrenalin clysmata sometimes relieves them. The diarrheas seen in vagotonics appear to be referable to the same cause as the spastic constipations.

Individuals who suffer from spastic constipation have the same type of contracted transverse and descending colon as that just described. A characteristic of this form of constipation is

¹⁵ Holzkecht, G., Münch. med. Woch., 1909, No. 50.

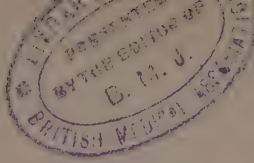
the inconsistency between the amount of the ingested food and the amount of the stool. This latter is usually hard, dry, marble-shaped and scanty. This is due to the fact that there is increased absorption of the chyme. In many cases, the small masses of stool are covered with mucus and seem wrapped in fat. This suggests an increased secretory activity on the part of the lower bowel, particularly since this condition so nearly approaches that of mucous colitis or a membranous enteritis. This latter is surely to be regarded as a secretory neurosis of the intestine since atropin has such a markedly beneficial action upon it.

The condition known as eosinophilic catarrh of the intestines is probably related to this disease and perhaps this is similar to bronchial asthma with its sputum rich in eosinophiles.

If we wish to attempt an explanation of spastic constipation in terms of autonomic stimulation, we must not forget that an important factor in this disease is an increased absorption of chyme, or a decreased production of mucus by the intestines. It need only be recalled here that the intestine will push forwards a large marble introduced into its lumen better than a small one, of which it can scarcely get rid. The probability that spastic states play a part is increased by the fact that atropin can rarely be dispensed with in these cases. Most probably the autonomic stimuli influence the activity of the intestine through an action upon the circular musculature, much in the same way as they do in increased stomach tone. Just to what degree autonomic stimuli play a part in increasing absorption of chyme [better absorption or digestion] remains to be investigated. It is possible that these autonomic stimuli cause an increased production of ferments.

Spastic constipation is often combined with spasm of the sphincter recti. This latter is often the principal complaint of the patient, and may in itself disturb the emptying of the bowel, owing to fear of the pain produced by defecation. We have noticed this symptom where there was neither fissure nor rhagades. These cramps in the rectum may be increased by certain diseases such as tabes, or may be the most important symptom of the disease, or may attract attention as a solitary symptom—coming in the form of crises.

Disturbances of the rectum are not infrequently associated with disturbances in other parts controlled by the pelvic nerve. Those patients who complain not only of spastic constipation



but of anal cramps during defecation, are frequently disturbed by erection and prostaticorrhea occurring during defecation, and probably many functional dysurias, such as pollakiuria, tenesmus, and dribbling are due to the same mechanism. And here must be included cases of "Trabekelblase" [predominance of the action of the detrusor muscle supplied by the autonomic system] which occurs as an early symptom of tabes. The fact that atropin has no effect in any of these disturbances except sphincter spasm corresponds with experimental observations that the pelvic nerve, which atropin should influence, is the great exception to the rule. On the other hand, pilocarpin irritates that nerve. We have observed spermatorrhea—though infrequently—as a consequence of an injection of pilocarpin, particularly in psychopathic individuals.

GALL BLADDER AND DUCTS.—It is very difficult to say whether the spasms occurring in the gall bladder and ducts are always of lithogenous origin, and not frequently of nervous origin. We have seen a case which came in with all the signs of a cholecystitis and which on operation showed a gall bladder free from stones and inflammation. That spastic condition of the gall duct play a rôle in the etiology of jaundice is shown by many observations of cases having cholecystitis.

We have seen cases in which operation has early shown that it was impossible for a stone to leave the bladder, and yet these cases showed jaundice at the height of the attack. The stool had been acholic up to this time. It is quite possible, that just as the spasm of the gall-bladder may evoke changes in both stomach and intestines, even causing pylorospasm, so it may produce spasm in the bile ducts, particularly the common duct, causing a transient occlusion of the lumen. The bradycardia so often accompanying gall-stone colic as well as the condition of the stomach and intestines shows clearly that the vagal system is being irritated. Such spasm may thus become the etiology in the nervous spasmodic jaundice described by Chvostek. Atropin has an excellent sedative effect upon the spastic conditions in these cases. But here it is quite worth noting that the usual doses of atropin are often insufficient to dissipate the colic [very hyperactive vagus].

It is quite possible that similar conditions may exist in the smooth musculature of the kidneys and urinary passages. We refer particularly to reflex anuria, which may possibly be asso-

ciated with spasm of the renal vessels. Hans Meyer¹⁶ raises the question of spasm of the renal canals in this connection. Experimental observations to determine the influence of the autonomic system upon the renal secretion are lacking. But this fact seems significant to us. Adrenalin, though it constricts the renal vessels, will cause polyuria [Jonescu]. We know that the same occurs in man. But, polyuria in man is by no means a constant result of giving adrenalin, and most probably is produced only in sympathicotonic individuals.¹⁷ Some have tried to include orthotic albuminuria as a manifestation of a vagotonic constitution [H. Pollitzer]. We have no individual experience relative to the correctness of this opinion. As symptoms of vagotonia on the metabolic side may be mentioned the lack of glycosuria after adrenalin as well as a high tolerance for dextrose—250 to 300 grams being assimilated without any resultant glycosuria.

Finally, there is a change in the blood picture which may develop on the basis of vagotonia. This is eosinophilia. It has already been shown that pilocarpin will evoke this while atropin will dissipate it.¹⁸ It is a frequent accompaniment to vagotonic stimulation and occurs very frequently in disturbance of the skin, intestines and lungs. Increase up to 5 per cent. occurs in other vagotonics as well. In individuals with sympathicotonia this eosinophilia is entirely lacking.

When we discuss, in the pages to follow, such diseases as spastic constipation, bronchial asthma, etc., it will be shown:

1. That the majority of the symptoms of these diseases are to be referred to autonomic stimulation.

2. That, besides those changes in the tone of the autonomic system directly responsible for the disease, there are also symptoms in other parts of the same system which are not manifestations of spasm but of increased vagus tone, as for example, bradycardia, hyperidrosis, etc., which leads to the opinion,

3. Those having a constitution which shows signs of general or local increase of autonomic tone are not infrequently found,

¹⁶ Meyer, Hans, und R. Gottleib, *Die experimentelle Pharmakologie*, 1910, p. 292 et seq.

¹⁷ *Translators' Note*.—See Falta, W., Newburgh, L. H., and Nobel, E., *Ueber die Wechselwirkung der Drüsen mit innere sekretion, Über Beziehungen der Ueberfunction zur Konstitution*, Z. k. M. V., 72, p. 2101.

¹⁸ *Translators' Note*.—See W. W. Herrick's article, *Arch. Int. Med.*, V, 13, 1914, p. 794.

and form a class which is predisposed to the most varied kinds of diseases.

4. Such manifestations of increased vagal tone may show in the entire system or its ramifications, or in a single branch general or local vagotonia.

We shall now proceed to the consideration of these constitutional anomalies.

6. CLINICAL PICTURE OF GENERAL VAGOTONIA¹⁹

We have been able to separate from the mass of nervous diseases, which have hitherto been grouped under the names of neurasthenia, hysteria and nervousness, a symptom-complex, a disease picture which we have designated the neurosis, "*vagotonia*." This we regard as a functional, *autonomic system disease*, for the reason that all its symptoms may be identified with those of a state of stimulation of the extended vagus [autonomic nervous system]. As the basis of this there must exist a *vagotonic disposition* in the patient, that is, an abnormal irritability of all or only a few autonomic nerves, which, under the influence of some adequate stimulus, a stimulus which may be less than that which would affect a normal autonomic system, may lead to the development of the symptom-complex *vagotonia*.

Furthermore, if we consider all the symptoms which are united in one disease in a given patient, as, for example, in nervous dyspepsia, gastric ulcer, cardiac neuroses, or Basedow's disease, we are struck by the daily finding that never, in any given case, do all of the symptoms of the disease appear, but that, apparently for no reason, we find sometimes this, sometimes that symptom standing out more prominently. We shall show, by means of well-known diseases, that the common bond between the apparently unrelated symptoms is the predisposition to vagotonia which is responsible for the ready activity and increased tone of the autonomic nerves. The disease itself as an etiological factor is to be contrasted with the constitutional predisposition, which in this particular case is the predisposition to vagotonia which implies an exceptionally ready irritability in the autonomic nervous system. On this account vagotonic individuals will in the

¹⁹ The attempt to present our views in the form of a small monograph does not permit us to introduce many detailed histories. Furthermore it has not been possible to include all of the pertinent literature.

course of a disease react to the poisons of the disease with different symptoms from non-vagotonic individuals.

On the one hand, the vagotonic constitution may be the basis of a neurosis which may be separated from the group of neurasthenias, while on the other hand it may modify in a definite way the course of various organic diseases. As a matter of fact, many symptoms may be referred to autonomic stimulation, and it is the regular relationship of certain symptoms such as asthmatic attacks and eosinophilia, which may be interpreted in the light of the conception of vagotonia. It is an old diagnostic principle to relate as many as possible of the symptoms to one cause, and we shall be in a position to attribute many symptoms to one cause.

Finally, the recognition of the physiological entity of the autonomic system must lead us, when we find one symptom of autonomic hypertonus, to look further for others, a principle whose heuristic and consequent diagnostic significance is without doubt most enlightening.

A. THE VAGOTONIC DISPOSITION.—How does the picture of vagotonia in man present itself to us? We have to do principally with youthful or middle-aged individuals. Both men and women come to us complaining of some trivial symptom, stomach or intestinal trouble, fear of heart failure, or some "neurasthenic" trouble and are treated as ambulatory patients. The appearance of these people is that of "nervous invalids." Their actions are hasty and precipitous. The color of their faces is often very changeable, now flushed, a troublesome condition for the patient, now fading into paleness. A similar thing may happen when the patient is asked to undress. When they do this, blotchy areas of redness may appear on the skin of the trunk, and arms, which seem to be of a considerable hardness. The hands of these patients are bluish-red, markedly cyanotic, getting pale when stroked by the finger, damp and cool. Of all of these conditions the patient often makes mention. The palms have a thick skin, although the patient may not have been doing any hard work. These patients complain that they perspire readily, and even over the entire body. In some there are places of predilection for the sweating which are quite characteristic (back, head, face, feet), and often during the examination of this class of patients the sweat rolls from the axilla down the thorax.

Under the influence of anxiety or excitement, the face rapidly

becomes moist, and drops of sweat appear on the forehead or nose after mild excitement. Sometimes, one can recognize a vagotonic as he enters the room. Large, often beautiful, eyes, which seem particularly large owing to the widening of the palpebral fissures, give the face an appearance which almost looks like that of Graves' disease. The eye glistens. Usually these people are undernourished, of inferior make up, who with their thick lips, plump nose and somewhat enlarged cervical lymph glands suggest that they may have had scrofula in childhood. Often the anamnesis justifies this impression. The skin of the back often shows fresh eruptions, often scars of an old acne, comedones, on the head seborrhea or scaliness is frequently found. The skin as a whole is moist and never presents the peeling conditions seen in old people, and in young people with severe diabetes.

The mucous membrane of the conjunctivæ is pale, or much reddened by intercurrent conjunctivitis. The palpebral fissures are as has been already stated, usually wider than normal, and as a rule one may see sclera both above and below the corneal margin. These people are often short sighted, and have mild anomalies in the muscular control of the eyes, there being a moderate degree of convergent strabismus. These anomalies show distinct variations parallel with the decrease or increase in the attention of the patient. (If there is not a high degree of shortsightedness.) Although the degree of shortsightedness is not high, these patients can bring objects very close to the eyes, and read at very close range. If they are asked to fix upon a very near object, the ocular axes converge to the maximum, and can be maintained in this condition of extreme accommodation for a correspondingly long period of time. Weakness in the muscles of convergence, Moebius's sign, is never seen in vagotonics. It may or may not be found in Basedow's disease. On the other hand, v. Graefe's sign, described only in Basedow's disease up to now, is frequently found. While observing these patients, one notices how often they swallow while speaking. They usually say that they have much saliva in their mouths. The tongue is often very much fissured, thick and moist with large follicles at its edges. If it be protruded far out of the mouth, or if one feels the base with the finger, enlarged lingual lymph follicles are felt. The palate is often greatly arched and small, the uvula large, and deviates to

one side or the other. The tonsils protrude from their recesses, and are often so large as to meet in the mid-line. Their surface, often pink in color, is rugged, and concretions, the remains of a former angina, are often found in the tonsillar tissue. These patients say that they get sore throats after the slightest exposure. These anginas are not accompanied by many symptoms, and high fever is the exception, rather than the rule. The throat is often reddened, the surface uneven, granular and covered with phlegm. Not infrequently strings of mucus, or masses of pus from the posterior nares are found hanging on the posterior pharyngeal wall. The pharyngeal tonsil is often much hypertrophied and covered with a purulent exudate. These patients complain of having to breathe through the mouth at night, and of having a continuous sensation of snuffles, and of a stopped up nose. As children, they have usually been operated upon for adenoids, polyps or tonsils. An almost typical phenomenon is the much diminished sensitiveness of the posterior pharyngeal wall and of the entrance to the larynx to tactile stimuli. A tongue depressor can be moved all about the soft palate and pharynx with considerable pressure without a resulting gag or swallowing reflex. Suitable instruments may even be introduced to the pharyngeal opening without inconvenience to the patient, in striking contrast to the otherwise marked irritability. Van Noorden²⁰ first described this phenomenon in connection with "hysterical vagus-neuroses."

We wish to say that, on the basis of our observation, we regard this phenomenon as entirely unrelated to hysteria.

There are no characteristic findings in the neck. Powerful pulsations of the carotid are as plainly visible as those of the temporals. A suggestion of struma calls to mind a mild Basedoid condition.

The voice sounds hoarse and husky, is easily roughened and the action of the vocal cords is very powerful. Manifestations of a diminished tone in the rima glottidis, resultant upon a faulty closure of the apertures made by the vocal cords, contrary to the case with sympathicotonia, are never found in vagotonics.

Later, we shall make mention of the variations in the structure of the thorax. Respiration is often shallow and is diminished

²⁰ Von Noorden, *Hysterische Vagusneurosen*, Charité Annalen, Vol. 18, p. 249. Bucholz, *Vagusneurosen*, Diss., Berlin, 1892.

in rate. The patient frequently sighs deeply after which there is a long pause in respiration. At the same time the patient puts his hand to the precordium, becomes momentarily excited, complains of a feeling of pressure and an inability to expire. Anomalies of inspiration are also to be found when the lower limits of the lung are examined. It often happens that there are great variations in the position of the diaphragm. If one day the lower border of the lung be found to lie at the fourth rib on the right side, rest in bed will cause it to drop two intercostal spaces by the next day. If the heart seems very much excited on examining the interior thoracic wall, it may become worse when the lung borders are reduced. A pulsation may be felt and seen in the region over which the sounds of the pulmonic valves are best heard. And also, in the epigastrium and at the apex, a marked pulsation is noticeable, as is found when severe damage to the heart exists. The apex beat may be heaving and hard to depress, without there being any anatomical lesion of the heart. The heart sounds are clear, loud, often split and rapid, the pulmonic second sound much accentuated and sometimes also split. Percussion shows no abnormalities. Only when the pulmonary hepatic border is particularly high can one find a slight increase in the dulness to the right.

If the patient remain quietly in bed for a few hours, the cardiac excitement subsides. Sometimes a persistent thymus is demonstrable both by percussion and X-ray. The activity of the heart, as shown by its rate, may vary greatly. It is striking that even when patients of the nervous type which is being described, are under stress of excitement, the heart rate often does not rise above 60, and may even be less. However, the patients will often say that the rate of their heart increases paroxysmally, and that it is in these periods of relief from bradycardia that they feel better. At times, there is a feeling as if the heart would cease beating entirely, or that it is very irregular. These times are exceedingly trying for the patient. Accompanying these sensations there is often one of a wave of blood passing upward through the neck and into the head. Feelings of pressure over the heart cause the patient considerable discomfort. The lability of the cardiac action, a phenomenon which may be discovered both by auscultation and by palpation of the pulse, is most striking. Small and large pulsations follow one another, not always

in rhythmic sequence, and very slight exertion as, for example, getting up or walking about, suffices to cause a sudden transition from a bradycardia to a tachycardia. At times quite the opposite may be found—as for example the bradycardia which Erben²¹ found after kneeling.

The respiratory changes found in the pulse are also very striking. Deep inspiration will cause slowing at first, followed at the height of inspiration by acceleration. In expiration, the heart beats more rapidly than in inspiration. The vagotonic may suffer from arrhythmias, particularly after a heavy meal. Such arrhythmias may appear in susceptible people after drinking one or two glasses of carbonated water. It is easy to see that the transition from these apparently physiological conditions to that of a true cardiac neurosis is very simple.

The gastro-intestinal tract gives evidence of many abnormalities as well. The vagotonic declares that large pieces of food stick back of the heart after swallowing. Soon after beginning a meal feelings of fulness and distention come over the patient, though his appetite is not yet appeased. Sometimes the abdomen is seen to swell in the gastric region under the left costal margin. Relief is obtained by belching which is brought about by taking some bicarbonate of soda. Others complain of acid retching which may even attain the severity of heart burn. The appetite is variable though generally very good. The activity of the bowels is sluggish, yet now and then there are periods of unaccountable diarrhea to which the patient pays little attention, since in their experience these attacks had hitherto been a great relief. Stools are few in number and seldom bulky. These people know very well that if their diet consists largely of vegetables, and other foods rich in residue they are less costive and have fewer troubles. A diet almost exclusively made up of carbohydrates is very poorly borne, since it is just this diet which gives the sensation of pressure in the stomach. The abdomen as a whole shows little that is at all characteristic. The sigmoid, filled with feces, but rarely very thick, frequently may be felt. Coils of intestine, tightly stretched out, or filled by pseudofecal tumors are rarely to be found in these individuals. Splashing

²¹ Erben, S. Ueber ein Pulsphänomen bei Neurasthenikern. *Wien. klin. Woch.*, 1898, No. 24.

in the region of the stomach directly after eating or after drinking a great deal of fluid is also very infrequent.

Vagotonics pass their urine in small amounts and at frequent intervals. It is, as a rule, brightly colored and may precipitate out a "sedimentum lateritium" in cold weather. Frequently an abundant nebula is found. Besides this the urine is rich in oxalic acids. It is sometimes excreted as a cloudy fluid due to an overabundance of phosphates, or, at least, precipitates the phosphates after excretion.

These urinary conditions are associated usually with urinary hyperacidity. This seems all the more probable since it is just where gastric hyperacidity is found that we run into these conditions. Usually there is also found an excess of carbonates in the urine and particularly after meals it may form on addition of acids. In many cases, there is slight dysuria, the patient having to strain or wait a few minutes before the urine can be voided. Other patients declare that the stream is broken. Dribbling after micturition has ceased is often admitted after questioning, much as is the case with the other symptoms, which we have described as characterizing the vagotonic.

The vagotonic is often sexually very excitable. Erections of the penis are frequent though of short duration. Premature ejaculation often occurs. Others complain of frequent pollutions.

Certain nervous stigmata are almost always present. The tendon reflexes are increased. Sometimes Chvostek's sign may be obtained. The cremasteric, abdominal and muscle reflexes are active. Tremor of the eyelids and tongue, as well as of the extended fingers is almost never absent. Dermographism is usually marked.

Most of the symptoms which have been described give the patient no trouble at all, and are only discovered after careful questioning. Many latent signs of autonomic irritation are first found in this way, and thus lead on to further search. In the domain of the vascular system, reflexes are often obtained which we have just discussed, bradycardia after pressure upon the eye, or stimulation of the nasal mucous membrane by ammonia, tobacco smoke, etc. If atropin be dropped into the eye, marked mydriasis and disturbance of accommodation result, while if pilocarpin be used, there result uncomfortable feelings besides the accommodation spasm. The stomach is much contracted. Fre-

quently a striking hyperacidity begins. Findings of 70-100 Riegel units after a test meal of three pieces of zwieback and 300 c.c. of water (removal in 40 to 45 minutes) are not at all unusual. The stool estimated by its condition in any twenty-four hours is scanty and poor in water and often has the form seen in spastic constipation. If the tone of the sphincter ani be tested with the finger it is often found much increased, there being a strong resistance. Pneumographic curves show irregularities in respiration, while the sphygmogram shows the respiratory conditions which have already been described, and spirometric curves show the type of respiration above mentioned. The blood shows an eosinophilia. For the sake of completeness, the results which are obtained with pilocarpin (.01 gm.) and adrenalin (Parke Davis, 1 c.c.) subcutaneously administered will be noted. After the former, the vagotonic salivates and sweats profusely, while after the latter there are scarcely any subjective symptoms, and in the typical vagotonic neither polyuria nor glycosuria. People so constituted are found in large numbers in the dispensaries if the trouble be taken to find them.

It is but natural that there are not many who will show all the signs and symptoms which have been described, yet we have found types which nearly do. It is interesting to add that vagotonia may be a family stigma.

The term which we have coined for the constitution showing an overactive or overirritable autonomic system is *General Vagotonia*, and we feel that this must be distinguished from *Local Vagotonia*, in which vagotonic symptoms are to be found only in some single system of the body, nor is it a matter of little interest that vagotonia may be very marked in but a single branch of the autonomic system, in accord with the physiological divisions.

Cases have been found in some of which the cranial, in others the sacral parts of the autonomic system show the most marked signs of irritation.

B. PATHOLOGICALLY INCREASED VAGOTONIA.—Pharmacological testing of various individuals shows that after the administration of pilocarpin conditions occasionally result which resemble very closely certain entities which we have learned to recognize clinically. Thus, after such an injection, gastric symptoms appear resembling those of hyperacidity, or those of pylorospasm, or cardiospasm, or it may happen that heart symptoms

resembling mild angina pectoris are found. In other cases, there are respiratory disturbances, salivation or even asthmatic attacks. In connection with the injection diarrheas, urgency in micturition or defecation, spermatorrhea, lachrymation, ptyalism or sweating may also appear.

These manifestations following pilocarpin injections lead us to believe that such diseases which in their fully developed form are known as angina pectoris vasomotoria, bronchial asthma, cardio- or pylorospasm, gastro-succorrhea, gallstone colic, tenesmus, etc., are genetically related to each other, inasmuch as they all may be induced by toxic agents which act upon the autonomic nervous system, and furthermore it would seem that they are both made manifest due to the basic vagotonic disposition of the patient which favors their appearance. In many cases, it is demonstrable that not only will atropin relieve the symptoms of the disorders just mentioned, showing that they are due to vagal irritation, but that latent manifestations of vagal irritation come to the surface in branches of the autonomic system other than those primarily involved in the disease.

Bronchial Asthma.—That the asthmatic paroxysm, with its characteristic expiratory dyspnea, and its tenacious sputum filled with eosinophils and Charcot-Leyden crystals, is due to vagal stimulation has already been stated. It may be worth repeating here that peripheral stimulation of the vagus in animals will produce asthmatic attacks with bronchiospasm. In one case v. Schrötter, Jr., while performing laryngoscopy, saw a sudden narrowing of the lumina of the bronchi. This necessitated stopping the examination. Subsequently there developed a quite typical attack of asthma. This so-called nervous asthma is to be compared to those cases in which the vagal irritation is due to some local anatomical stimulation, as enlarged bronchial lymph glands due to tuberculosis or to carcinoma of the bronchi (A. Schmidt).

In connection with the asthmatic attacks there may be nervous symptoms referable to other branches of the vagus, such as sweating, dermography, urticaria factitia, bradycardia, sometimes lowered blood pressure, uncomfortable feelings in the stomach or intestines, positive v. Graefe, or laryngospasm due to closure of the rima glottidis. That the pulmonary branches of the vagus are over-irritable, may be shown by the variations in

pneumographic curves taken between attacks. Besides it may be shown that after deep inspirations the spirometric curve does not sink at once, but descends gradually to its former level. As asthma may be relieved by atropin or adrenalin, so also may the symptoms which accompany it. Laryngospasm is closely related to asthma and we are surprised that atropin has not been tried for relieving this condition in children. The most severe form of laryngospasm is found in tabes, usually as an early symptom and, as we have been able to observe, this is frequently associated with other symptoms of vagal irritation as lachrymation or sweating.

Vagotonic Diseases of the Stomach.—Stimuli may act upon the autonomic supply to the smooth muscle and secretory apparatus of the stomach, and may produce pathological states of the same nature as are found when the autonomic system is in a state of increased irritability. The severity of the subjective symptoms is frequently the only deciding point, since we have found that the objective signs in the stomach are the same whether the patients complain of them or whether they are found during clinical examination for the purpose of finding vagotonic manifestations. Frequently we find the pathological condition gradually modifying itself into a pure vagotonia. This applies particularly to motor neuroses. In a series of cases showing signs of vagotonia outside of the domain of the stomach, and in which patients complained of pressure in the region of the stomach, rumblings in the stomach or cutting pains after eating, the X-ray examination showed that the peristaltic action of the stomach was much increased. Often we observed that the stomach filled slowly; as soon as the bismuth appeared at the fundus there appeared a strong wave of peristalsis which apparently cut the bismuth into two parts. Not infrequently, the stomach seemed to be separated into three ball-like partitions. This condition may be observed for varying lengths of time. Sometimes the stomach emptied promptly without there being any lengthening of the usual time. In other cases, antiperistaltic movements appeared before the stomach emptied itself. This pointed to a spastic condition of the pylorus, particularly since there was as a rule no evidence of motor insufficiency. These conditions are sometimes so plain that they may be seen on the surface of the abdomen. But since they are, as a rule, associated

with an increase in the tone of the gastric musculature, they are not always observable on simple inspection of the surface of the abdomen. Yet it is just in these last mentioned cases that we find a valuable point of differential diagnosis from the increased peristalsis due to mechanical obstruction.

I. H., a girl aged 27, who had previously been treated for "stomach trouble," has since an emotional shock been vomiting everything which she has eaten. At the same time she has suffered from hunger. As soon as she eats, she experiences a feeling of pressure in the region of the stomach. This feeling leaves as soon as she vomits, which usually takes place 3 to 4 minutes after eating. After being six weeks in this condition, she lost considerable strength. The girl looks much emaciated and pale. The glands of the neck and throat are enlarged. The pharyngeal reflex is absent. Pulse rate 64 to the minute, which does not increase during vomiting or after the excitement subsequent to it. There is *pulsus irregularis perpetuus*. Eosinophils 4 per cent. Marked dermatography. Stools while the patient was well were always small in amount, and sometimes covered with mucus. The patient was costive, though always being used to it she never found this condition a cause for complaint. X-ray examination of the stomach showed that the bismuth passed rapidly through the esophagus to the stomach. The meal remained longest in the fundus. Though the patient ate quite rapidly and the fundus dilated considerably, there was but a small strip of bismuth visible at the caudal end of the stomach. The picture changed but little after 3 to 4 minutes and no bismuth was forced toward the cardia. The patient soon complained of severe pain, and gradually peristaltic waves appeared in the fundus, after which vomiting became imperative. Some of the bismuth remained in the stomach. After the lapse of about an hour, shadows of bismuth were seen in the pyloric region. A test meal was impossible. There was no blood in the stool.

The patient was given .001 grain of the sulphate of atropin daily. On the day following the commencement of this therapy, there was no vomiting. An X-ray showed that the bismuth meal was still held in the fundus for a considerable time, but after three minutes passed caudalwards (towards the pylorus) in a strip a finger's breadth in size. As this strip gradually widened, the mass passed on to the pylorus. This was reached in eight minutes, whereupon strong peristaltic movements began. There is but small wonder that on the basis of a faultily interpreted X-ray this case seemed to be one of hour-glass stomach and gastric ulcer before it was more carefully examined in the clinic. Atropin therapy was continued. In three days she could eat everything, and in five more left the hospital cured.

At the beginning of this section we called attention to the physiological distribution of the ingesta of the stomach. In many cases the sojourn of the ingesta at the entrance of the *pars media* is so long that a single roentgenological inspection readily gives the impression of an hour-glass stomach. This spastic hour-glass stomach is found now and then in those who complain of the most varied functional gastropathies. And it is only too frequently that one hears these patients say that they can eat but small amounts of food at a time, or that they must stop eating during meals to prevent pain or even vomiting. When the beneficial action of atropin is seen in such cases, and its effect upon the

X-ray picture, it becomes apparent that there must be some relation between autonomic stimuli, and gastric neuroses. The recognition of this relationship is of particular diagnostic importance since symptoms similar to those found in these functional gastropathies are also found in gastric ulcers. Not only is this true, but it is also true that both ulcer and neurosis may be found together.

A. K., a shoemaker, 45 years old, has been complaining of vomiting during the last five months, while previous to that he had always had stomach trouble. Recently he has been vomiting blood-tinged material. Since blood was always found in the stool, since the vomitus was found to be very acid, and since X-ray examination showed that the bismuth meal remained a long time in the fundus, and did not move on after 3 to 4 minutes, a diagnosis of gastric ulcer and hour-glass stomach was made, and an operation was performed. On opening the abdomen it is true there was a large ulcer on the lesser curvature while not the slightest evidence of hour-glass stomach was found. It is certain that more careful investigation of the case with subsequent atropin therapy would have eliminated this gastric spasm.

The symptom complexes of what seem to be nervous cardio-spasm or pylorospasm are frequently found as diseases associated with general vagotonia. And here too the variability of the accessory symptoms is very striking, in that they occur sometimes in one, sometimes in the other part of the autonomic nervous system. At any rate it was noticeable that a relationship to vagotonia had to be considered in all the hyperkinetic neuroses of the stomach. The opinions of many authorities on the favorable action of atropin upon the gastric neuroses speak in favor of our view of this question. This opinion we can confirm and can recommend this remedy in all hyperkinetic gastric neuroses. Besides this, we feel that all those neuroses which are associated with increased gastric secretion are referable to stimuli from the autonomic nervous system. As in the discussion of motor disturbance so here also do we find there are often great difficulties in distinguishing between true pathological conditions and those which are but part of a general constitutional make-up. The symptom hypersecretion or hyperacidity alone cannot be the only one to give trouble. As we shall show later on, the symptoms of gastric hypersecretion are often associated with those of hypertonicity. The more symptoms referable to autonomic stimuli which we find the more readily may the diagnosis of such cases be made. Later we shall remark upon what seem to be exceptions to this rule. When one observes how the signs of increased activity of smooth muscles and of glands particularly of the

stomach seem not unlike in both normal and pathological conditions, and can be distinguished only by the subjective sensations which give rise to the trouble, one is convinced that in the truly pathological condition some further condition must exist. Since in some cases hyperesthesia cannot be overlooked, the possibility presents itself that the sensibility of the stomach plays a considerable rôle. This opinion is partially confirmed by the observation that individuals who complain of the most varied types of gastralgias and who in addition have hypermotility and hypersecretion obtain great relief for their pain through analgesics, but none for the objective hyperkinetic symptoms. The newer results which have been obtained by the Förster operation in the gastric crises of *tabes dorsalis* strengthen the belief that sensory stimuli are of the greatest importance in considering gastropathies. Briefly it may be stated at this point that in many vagotonic states of stimulation there are found areas of hyperalgesia in the zones, described by Head. There is, however, no reason to believe that there exists any relation between vagotonia and a lower threshold to pain, in spite of the fact that these two manifestations occur together so frequently.

Dreyfus in an interesting review of nervous dyspepsias comes to the conclusion that in practically all cases which are truly of this group there is a psychoneurosis, and that this psychoneurosis is the primary cause of the condition. In the conclusions of his article he says, "The great question is now as it was before, how are the psychoneurotic conditions in the stomach produced, and how is it that they occupy the foreground?" When Dreyfus goes on to say "On that point we must admit not having a reply," we feel that the question is to be answered in laying the blame on a constitutional disposition to vagotonia. The histories of some of our papers have made this certain to our minds.

In conclusion, we wish to ask the question, why in some cases in which we find marked objective signs of vagotonia, as powerful gastric peristalsis and hyperacidity of marked degree, some complain of gastralgia while others do not have the slightest complaint to make? When we consider that both the autonomic nervous system, and the sympathetic nervous system come together in the central nervous system, and when we realize that not only stimuli but also inhibitions (cf. Psychoses) come from them, we must not forget that in nervous disturbances of

visceral nature, pathological conditions in the central nervous system cannot be left out of account.

Nervous Diseases of the Intestines.—Nervous conditions, due to increased irritability, are more often found in the domain of the intestinal tract than in any other visceral organ. Almost on the border between the normal and the pathological are those cases in which an over-irritable individual after some strong emotion, as fear or excitement, or after bodily exercise, as a railroad trip, or after being exposed to the cold, reacts with one or more fluid stools. These cases are surely not of organic basis, since the diarrheas disappear too rapidly, the course of the disaffection is afebrile, the appetite is undisturbed, and the patient as a whole feels excellently. The mildest form of this intestinal disturbance is found when, after one or another of the above-mentioned conditions, there ensues, in the absence of all pain, one or two fluid stools.

These diarrheas rarely last longer than twenty-four hours. When they do last longer they suggest the idea that what was in the beginning purely a nervous or functional disease has lost this character and has become an inflammatory disease of the mucous membrane. Those cases with nervous digestive weakness of the intestine, which Moebius first described, belong to this category. This disease affects neurasthenic individuals. They have several stools a day which are excessive in amount and either normal or very fluid in consistency. Pain is never a complaint in their connection. The transition from this condition to that of the chronic neurogenic diarrheas first described by Trousseau is readily understood. The fact that those who are afflicted with these abnormal conditions show signs of vagotonia in viscera, other than the intestines, seems to us to be very significant in the description of the malady. Besides this there is the evidence obtained by a comparison with the pilocarpin test. It is scarcely necessary, at this point, to reëmphasize the fact that various vagotonic manifestations may help us in diagnosing such a state in the intestines, *i. e.*, *neurogenic diarrhea*. Counted among these are, briefly, cardiac palpitation, accompanied by a feeling of anxiety, a general feeling of pressure in the chest, breathlessness and the sensation of not being able to expire, transient facial and general body hyperemia, tenesmus and, often, hyperacidity. Related to the group of neurogenic diarrheas are

states of intestinal peristaltic unrest. Individual experience has taught us of the active rumblings resultant upon intestinal activity. Under pressure of some nervous excitement, whose outlet travels most readily by way of the vagus, these intestinal movements assume the intensity of the so-called *peristaltic unrest* of the intestine. This is limited to the small intestine and does not manifest itself as a diarrhea, but as noisy rumblings and, in the case of individuals with thin abdominal walls, as visible intestinal movements, most readily made out in the umbilical region. Certain therapeutic measures cure those neurogenic diarrheas seen in Basedow's and Addison's diseases. Opium and astringents are as a rule without effect. Atropin is not a good drug to use in Basedow's disease since, even when administered by rectum, it spreads very rapidly through the body and produces undesirable by-effect. Belladonna preparations are of more service. Adrenalin enemata produce very gratifying results (20-30 drops of a 1-1000 solution in 5-10 ounces (150-300 c.c.) of water). Adrenalin, even when given in large amounts, is but slowly absorbed from the intestinal tract, and gives no undesirable symptoms, never producing a tachycardia, while it does seem to diminish peristalsis when locally applied.

This same therapy is applicable to the diarrheas of Addison's disease, provided they are due to toxic conditions and not to tuberculous ulcers or intestinal catarrh. The varying behavior of the evacuations occurring during tuberculous ulceration of the intestines shows how large a rôle the neurogenic factor, that is, the irritability of the autonomic nerves to the intestines, plays in the production of diarrheas. There are cases of tuberculous ulceration of the intestines, which lead to uncontrollable diarrheas, while there are others in which the regularity of the evacuations leads to not the slightest hint of any tuberculous disease of the intestine. That there is some degree of underdevelopment of the chromaffin system in tuberculosis and a consequent over-irritation of the autonomic system, even though there is no question of Addison's disease, seems, on the ground of many observations, to be without doubt.

Myeloid leukemia and many cases of lymphosarcoma (not only of the intestine, but of other regions) are often complicated at their beginning by a combination of persistent sweating and uncontrollable diarrheas.

While considering intestinal disorders, it may be permissible to put in a few words about acid jejunal diarrhea. We do not wish to discuss the pathological basis of this singular intestinal disease, but merely to call attention to the fact that the increased peristalsis and the frequent complication of gastric hyperacidity recall a state of increased irritation in the autonomic nervous system. Due to the increased production of acid, the digestion of starches is hindered, more work is required of the intestinal tract and at the same time the acid ingesta mixed with the undigested carbohydrate becomes a stimulus to the intestinal mucous membrane. Atropin to counteract the hyperacidity and restriction of the carbohydrates are good therapeutic measures for this kind of fermentative dyspepsia. It must be left to further investigations of these cases to discover other symptoms referable to autonomic hypertonia.

Mucous colitis often develops on the basis of a long-standing habitual constipation. There are transitions between true mucous colitis and membranous enteritis (true inflammation). Mucous colitis, in the narrower sense, is an intestinal neurosis, in which an anomalous secretory activity exists in addition to the increase of peristaltic action. The stools are mixed with an abundance of mucin. When we consider this disease we almost involuntarily think of the action of pilocarpin upon the intestine of rabbits. At the height of the action of the pilocarpin the animal evacuates not only large amounts of feces, but also characteristically glairy, tenacious mucus which is as coherent as a band. Our viewpoint is strengthened on considering that atropin has proved a most efficacious therapeutic agent in mucous colitis.

Eosinophilic catarrh seems to be the analogue of mucous colitis, occurring in more distal parts of the intestinal tract. This disease resembles mucous colitis in all but one of its characteristics (eosinophils). Its name recalls the relation to eosinophilia of other diseases which symptomatologically and etiologically appear to be due to autonomic irritation, as, for example, bronchial asthma and Teichmüller's eosinophilic catarrh. Not only in mucous colitis but also in eosinophilic rectal catarrh²² were we able to find evidences of vagotonia. This was found in the most distal segment of the intestine as well as in other parts, in which

²² Neubauer, O, and Stäubli, Münch. med. Woch., 1906, No. 49.

it manifested itself as salivation, bradycardia, a tendency to sweat, etc.

A laborer, age 27, noticed for the first time two years ago that at the end of defecation, there appeared bright red blood mixed with mucus. For the last six weeks he had had frequency of defecation, accompanied by distention and sensations of gas in the abdomen. Pure blood unmixed with feces is sometimes expelled with the gas. The blood is yellow-red, and is often intermingled with streaks of darker blood. At these times the stool is retained.

The patient looks healthy, the mucous membranes are a bit pale, the hands are moist, perspiration appears on the face and head at the slightest physical exertion. Pulse rate 64-80, tonsils large, not reddened. Internal organs are normal. The stool, which is firm, is surrounded by a slimy purulent coating, which is shiny and thick.

This shows on microscopic examination, shreds of mucus, epithelial cells, lymphocytes, blood corpuscles and very many eosinophils. Rectoscopic examination shows a dark-red mucous membrane with a patchy appearance. On this surface are many large and small yellow-white masses. Microscopically, these prove to be a mixture of eosinophil leucocytes, extracellular granules and Charcot-Leyden crystals. Blood examination shows an eosinophilia of 6.3 per cent.

Pharmacological Tests.—Pilocarpin gives a strong reaction, atropin a moderate reaction, adrenalin causes neither glycosuria nor vascular symptoms.

Spastic constipation is a frequent finding in vagotonic individuals. Since atropin has a very favorable effect upon this condition, moreover, since spastic states in the circular colonic musculature are certain and spastic states in the rectal sphincter are known to play a part, we are inclined to attribute this disease to autonomic irritation. Several signs are necessary for a diagnosis of spastic constipation.

These are: diminution in the volume of stool combined with diminished water-content and perhaps increased resorption; spasm of the circular muscle and frequently an increased secretion of mucus in the stool.

On casual observation it would seem foolish to ascribe two such opposite conditions as constipation and diarrhea to the same cause. We believe, however, that the same etiological factor is operative, only in one instance the circular, in the other, the longitudinal muscle is affected. We find a similar state of affairs in the stomach, for here also spastic states and hypermotility are referable to the same underlying cause. At all events the behavior of the nerves to the intestines are exceptionally complicated, due to the presence of the mesenteric plexus. Besides, an attempt should be made in each case to separate peripheral from central vagal stimuli. Many observations in pharmacological literature show that there may be important differences in this

connection. The frequent occurrence of spastic constipation in vagotonia, the above-mentioned beneficial effects of atropin, and finally the not unusual transition from a spastic obstipation to a diarrhea, leaves this idea of its cause on firm ground. The complete comprehension of this disease must be left to further researches.

The vagotonic manifestation of irritation in the domain of the *heart* may be very varied. The most dangerous disease, which may involve the heart, due to increased vagal impulses, is a disturbance in the transmission of the cardiac impulse—conduction disturbances—or heart-block. As is well known this does not imply a complete interruption of the conduction of the impulse from auricle to ventricle, but a condition in which several auricular impulses occur before one finds its way through to the heart. Consequently the number of auricular beats is a multiple of the ventricular beats. In such individuals previous to or in the early stages of the disease, the heart rate is slow. It is typical of this disease that it may be relieved by atropin, while a true heart-block (Stokes-Adams disease), based on anatomical changes, that is, a complete dissociation between auricle and ventricle is but slightly or not at all affected. The pulse-rate changes but little or not at all. It is important to recognize this because it is in them that the vagotonic action of digitalis acts very unfavorably and may indeed produce some of the symptoms of the disease, while others it may aggravate (Wenckebach). Not only in these cases but whenever digitalis is used, there is often the chance to note the undesirable complications subsequent to its administration and due to its vagotropic action.

The relatively early appearance of bradycardia, and perhaps also disturbances of the stomach and intestines are signs that in certain individuals an exceptional irritability in the realm of the autonomic exists: atropin is an excellent adjuvant to digitalis therapy in such cases. Just as there are individuals who react to excitement by means of a physiological tachycardia, so also there are those who react in reverse fashion; that is by a bradycardia (neurogenic). This condition is frequently associated with diminished blood pressure, and by reason of a bradycardia and lack of cyanosis, may be differentiated from the organic insufficiencies of the heart, which are associated with tachycardia and cyanosis. It has been observed that this clinical syndrome ap-

pears in the course of, or during the convalescence of certain infectious diseases, both in the juvenile and in the adult epochs of life, particularly when a fatty heart exists. A particular form of bradycardial hypotonia is found in certain cases of exophthalmic goiter. (M. Hertz.)²³

There may also be a transient bradycardia in certain forms of goitrous heart. The vascular hypotonia as described by S. Münzer²⁴ may be a similar disease. Many of the clinical histories, which he has cited, strongly reminds one of the findings which have been made in typical vagotonics. It is also noteworthy that Münzer often found associated stigmata of status thymolymphaticus. It is well known that bradycardia always occurs when the tone of the vagus is altered by any organic process, as, for instance, neuritis or compression, or by peripheral stimuli, as, for example, tracheotomy, laryngoscopic examination, etc. Frequently there are manifestations of irritation in branches of the vagus other than those supplying the heart.

Angina pectoris vasomotoria is certainly neurogenic in origin. If it is to be considered as a spasm of the coronary vessels it becomes necessary to regard the spasm as due to an increase of vagal stimulation since the constrictors of the coronary vessels are innervated by the autonomic nervous system. It is just the nervous form of angina pectoris, which is associated with many other manifestations of vagotonia, a fact which makes it difficult to regard this disease otherwise than we have suggested.

Similar nervous influence may be a causative factor in organic stenocardia, and it is just in this disease that we may find vagotonic manifestations of irritation as bradycardia, paroxysms of sweating, as well as gastric and intestinal symptoms. Later we shall discuss the etiological nexus, which exists between this condition and the climacterium in which the disease is frequently found.

Cardiac Neuroses.—The symptomatology of these conditions is very variable and it is exceptionally difficult to explain all their manifestations on the basis of a single cause. Marked lability of the heart action, variations in the pulse rate, even after the slightest physical or mental exertion, extra systolic arrhythmias and the very many other nervous manifestations, not of a cardiac

²³ Hertz, M., Über bradycardische Hypotonie, Med. Klin., 1910, p. 763.

²⁴ S. Münzer, Vaskuläre hypotonien, Wiener klin., Woch., 1910, No. 38.

nature, which belong in many cases to the picture of a cardiac neurosis, make it almost impossible in any given case to explain all its symptoms on the basis of a single cause. Thus it happened that Krehl²⁵ advanced the suggestion that it would be wise to collect clinical observations without considering the significance of the various nerves and ganglia of the heart until more knowledge should have been gained. But since pharmacological testing of visceral nerves has given us the opportunity to discover conditions of irritation in the two antagonistic systems, it appears possible for us to separate etiological principles for the cardiac neuroses on the basis of the tonus of the nerves regulating the heart action. In accord with this idea, we may postulate both a vagotonic and a sympathotonic cardiac neurosis. Finally it is conceivable that there may exist in both cardiac nervous systems a condition of hypotonia similar to that found in many cases of exophthalmic goiter and catatonia. It would be premature to give any final judgment, in this perhaps the hardest chapter of visceral neurology, yet it seems certain that there are cardiac neuroses in which all the symptoms are referable to an increased functional activity of the vagus. Thus there are cases, so-called neurasthenic cardiac weakness, in which besides painful sensations in the neighborhood of the heart there exist marked respiratory arrhythmia, even disappearance of the pulse during deep inspiration, cor mobile, dermatographism, enlargement of the tonsils, Aschner's pressure phenomenon and asthmatic attacks with expectoration of a tenacious sputum containing Curschmann's spirals. In these cases the point of maximal impulse of the heart is heaving and pushed outward. It is interesting that in such cases atropin may relieve not only the respiratory arrhythmia, but also the high grade tachycardia, a symptom which does not seem to belong to the same group as the others. The syndrome described by M. Herz,²⁶ bradycardial hypotonia, belongs also, according to our own observation, under the heading of vagotonia. Phrenodynia, temporary respiratory suspension,²⁷ irregularity of the pulse, marked mobility of the phrenocardiac heart, beside spastic constipation, which so often accompanies these, may all be considered part and parcel of vagotonia. It is

²⁵ Krehl, L., Ueber nervöse Herzerkrankungen, Münch. med. Woch., 1906, No. 48.

²⁶ Herz, M., l. cit.

²⁷ Herz, M., Die sexuelle psychogene Herzneurose (Phrenokardie), 1909.

our own impression also that certain cases of goitrous heart, with relative bradycardia, dermatographism, tendency to sweating, weak dicrotic pulse, moist eyes, and widely opened palpebral fissures, which conceal an exophthalmus, owe their existence to a preexisting vagotonic constitution upon which a secondary thyroidism is engrafted. These cases have been put under the caption of *Vagotonic Goiter Heart*.

Briefly stated, it may be said that we have tried to show in the foregoing pages that certain stimuli may be super-imposed upon a vagotonic constitution, and that these lead to diseases whose characteristic course shows that their most prominent symptoms are those of autonomic stimulation. The significance of this is that we learn to recognize a definite relationship between certain symptoms occurring in the most various organs, a relationship whose origin lies in etiology and that by means of apparently insignificant symptoms we are enabled to recognize the cause of a disease, and are enabled to influence it therapeutically.

For those in whom we feel that there exists a generalized disposition to the vagotonic state, as well as those in whom some disease of the vagotonic type has been superimposed upon a vagotonic constitution, there are frequently to be found certain stigmata which are not closely related to this constitutional anomaly, and which are not referable to the same etiology. However, these stigmata are of such frequent findings that they may almost be regarded as characteristic earmarks of vagotonia. They are so apparent that they often lead us to a diagnosis of vagotonia. We have probably made it clear by what we have said in the foregoing pages, that when we deal with vagotonics we are, as a rule, also dealing with "nervous" people. Neurasthenic and hysterical complaints are often the apparent basis of the trouble and so there is little cause for wonder at the fact that physicians have regarded the symptoms, which we have described as vagotonic, as the manifestations of an hysterical or neurasthenic constitution. Without entering into a discussion of the justification of confusing hysteria and neurasthenia with vagotonia, we may say that the hysterical component, at least, is often absent in many vagotonics. As far as the neurasthenic stigmata are concerned, it is worth saying that there is a definite group which may be separated from them, which can be accounted for on the basis of one etiology. This fact may throw

some light upon the condition known as neurasthenia, one which is often very variable and very difficult to circumscribe and diagnose. V. Noorden has described a symptom-complex which he has called—the *hysterical vagusneurosis*. His cases are in many ways similar to those we have described as vagotonic. Since in his cases certain stigmata could be regarded as of hysterical origin, and were generally included among the symptoms coming under the caption hysteria, it is natural that the emphasis should have been laid more on the side of that disease than on that of vagotonia. Typical of all his cases was the lack of the pharyngeal reflex. This symptom is, however, so frequent a finding in vagotonics, without any hysterical stigmata, that we are inclined to reject hysteria as the cause of it in these cases. On physiologic grounds, this symptom cannot be brought into relationship with vagotonia, since the region which is anesthetic when the pharyngeal reflex is lacking is supplied by the glossopharyngeal and trigeminal nerves.

Another symptom frequently found in vagotonics is moist hands and feet. Here also a physiologic explanation is difficult. It is relatively easy to account for sweating, but to account for the localization is not so easy, and all that may be said is that there is a localized stimulation of autonomic fibers. The erythematous appearance of these areas [extremities] is usually regarded as vasomotor in origin. But the relationship existing between vasomotor and visceral nerves is not yet entirely clear, though there is much evidence to prove that the vasodilators are supplied by the autonomic nervous system. From this point of view cyanotic, moist hands are signs of vagotonia. Hands so affected are often large and the fingers long and thin. The same applies to the feet, which, in addition, may be flat.

We shall attempt no explanation of myopia, a frequent finding among vagotonics. Enteroptosis is often found combined with the general nervous state of these people. Long, chest, costal fluctuantes, cor mobile, even cardioptosis, palpable kidneys, and even prolapsed uteri are also frequent findings. Both men and women may show some signs of enteroptosis. The abdomen is often small above, wide below, while the abdominal wall is lax and poor in muscle. Not infrequently the women have both a masculine form and a masculine distribution of hair. The pubic hair is not horizontally delimited, but extends upwards towards

the umbilicus. There may even be curly, upright hairs on the linea alba above the umbilicus. These women have small, under-developed breasts with large nipples around which a ring of hair may be found.

It is remarkable that we often find some evidence of a persistence thymus. Many vagotonics are of lymphatic constitution, as shown by the enlarged tonsils, large lingual follicles, as well as the solitary lymph nodes of the tongue, and by the condition of the lymphatic apparatus of the conjunctiva. Occasionally rectoscopic examination will reveal large lymphatic follicles on the rectal mucous membrane. As has been stated the tonsils are large, pale pink and much pitted.

We know full well that associated with the lymphatic constitution and persistent thymus is a diminution of the resistance to infection. The vagotonic also has a tendency to colds and other infections, and when infected has but very little resistance. Later on we shall discuss the possible etiological relationship between thymus persistence, the lymphatic constitution, and the vagotonic constitution. We may say at this point, however, that on X-ray examination we have been able to find a narrow aorta in a group of our vagotonic cases. We not only found anemia in this group of cases but also in vagotonics in general. The criterion for this was not alone the facial color, but the additional evidence of a blood examination. In fact a marked grade of anemia is quite characteristic of the vagotonic constitution.

When we discover that vagotonia is associated with so many other constitutional anomalies, which are manifestations of inferiority, we naturally are inclined to ask whether vagotonia itself is not a form of constitutional inferiority. That this view is true is strengthened by the fact that vagotonia is so frequently found in classes of people who show signs of degeneration, as, for example, Polish Jews.

Our contention that many diseases are related to the vagotonic constitution and that certain signs and symptoms are only produced when the proper soil is present admits of certain exceptions. As examples of this are certain cases of typical general vagotonia, associated with hyperacidity, diminished peristalsis and diminished gastric tone. It is also well known that spastic constipation, which is so frequent a finding in connection with

these signs of autonomic stimulation, may be associated with gastric atony. There are some cases in this group in which the gastric secretion is diminished. Finally tachycardia is often found present, while the gastro-intestinal tract and other visceral organs show signs of autonomic hyperactivity. These facts raise the question, can vagotonia exist in some parts of the visceral nervous system, while the reverse exists in others? Before entering into a discussion of this matter, we must outline our definition of vagotonia very sharply, and we must state that if we should find signs or symptoms which are significant of autonomic stimulation, as, for example, gastric hyperacidity, or nervous diarrhea, we would not feel justified in making vagotonia responsible for this symptom, without further inquiry into the case. For this symptom may be due to some organic condition, just as bradycardia may be of organic origin. Furthermore the symptoms referable to various organs, which are signs of autonomic stimulation, must have been spontaneously produced and not have been brought out by the action of drugs.

Thus we may say that vagotonia is a purely functional disease, not referable to any organic basis, which does not affect one organ alone, but spreads out, even if but transiently, in several branches of the autonomic system, until finally it involves them all and affects the entire autonomic system.

This definition of the condition as a functional disease narrows down the number of diseases which when having signs of autonomic stimulation might be considered as vagotonic. Looking at the matter in this way we are not inclined to consider every spastic state of the autonomic nervous system as a part of general vagotonia, even though it may be referable to autonomic stimulation, for if we did this and went so far as to say that every spastic state, which was in any way related to the vagus, was a sign of vagotonia, we should have to divide all people into the vagotonic and sympathicotonic, a procedure which would lead us too far afield. On the other hand if we did try to enlarge the narrow limits we have set for vagotonia and added to the not infrequent cases of this condition those which showed some signs which through being opposite to what was expected, spoiled the picture, it would but serve to increase the interest in this most important constitutional anomaly and throw more light upon visceral neurology.

Since true vagotonia may be associated with diseases of other etiology, organic or functional, certain groups of symptoms may appear in a given case, some of whose individual components will not fit into the picture of generalized vagotonia. Enteroptosis is very often associated with vagotonia and may be the cause of symptoms quite different from it. The tone of the organs within the abdomen, as, for example, the stomach, receives considerable aid through that of the abdominal wall. Should this latter be absent the smooth muscle cells are robbed of a valuable support. Vagotonics are just the class who, in connection with the symptoms of autonomic hyperactivity, suffer from various other complaints and pains, a fact which readily leads the patient into a state of malnutrition. The malnutrition affects the entire body, and this may affect the smooth muscle cells of the stomach. In a group of cases we saw that increase of the state of nutrition and general constitutional improvement bettered not only the gastric tone but also the secretory activity of the stomach.

Further difficulty in making a clear cut diagnosis of vagotonia is found in the symptom, tachycardia. This, we believe, is present in some cases due to enteroptosis, a relationship, which is most striking in cases of "cor pendulum." These people, who in every other way are true vagotonics, usually have a normal pulse rate when they are recumbent and breathing normally. However, the slightest exertion,—a tachypnoe of nervous origin for example—may cause a transient dyspnea which is augmented by the increased tone and relative narrowness of the bronchial branches. In enteroptotic individuals with long thoraces, this is followed by a very low position of the diaphragm, which in time, separates the heart from its proper support. This low position of the diaphragm, as well as changes in the position of the heart itself, are surely sufficient cause of a compensatory tachycardia. If one considers furthermore that secondary anemia is frequently present, and that autonomic stimuli may appreciably alter the distribution of the blood, it is scarcely to be wondered that this most important organ should exert itself in the interest of increased vitality. Only when the proper physiological requirements for the circulation are present, does the heart respond to autonomic stimulation.

7. LOCAL VAGOTONIA

In describing the syndrome of general vagotonia, we observed that an increase of tone could also occur in isolated branches of the autonomic system. This observation may not be in accord with what we have said up to now about localized vagotonia, but the fact remains that in the absence of local causes for the condition, a general state must be assumed of such a nature as to cause an increased tone in but one part of the autonomic system. Furthermore this state may exist even if there be no observable signs of disease or of increased irritation. Pharmacology has taught us that the various vagotropic substances have varying affinities, i. e., they affect different parts of the autonomic system with varying intensity [atropin for example]. So also, we believe, do metabolic poisons act, some causing an increase in tone in this part of the autonomic, some in that. It is in this sense only that we have postulated a local vagotonia.

It is to us a matter of no small interest, that on the basis of clinical observations, we have been able to find spastic states, affecting isolated parts of the autonomic, which may justly be called of true autonomic origin, and which seem to be associated with similar states in the particular branch affected.

Let us take spastic constipation as an example. This may be associated with symptoms which are limited to the pelvic nerve alone. One often hears that these costive patients have erections, spermatorrhea, or pain in the sphincters, associated with the attempt to defecate. Could we not suppose that the entire pelvic nerve is hyperirritable under these circumstances, and that it is stimulated by the act of defecation, so that, by an overflow of energy, the branches other than those supplying the rectum are involved. Furthermore, we have seen a group of cases in which epiphora, salivation and conjunctival asthma, as Rosenbach has described it, were associated, while in organs supplied by other branches of the autonomic no signs of stimulation could be found. In such cases we suppose that certain poisons, circulating in the body, have the the same partial action as has been found to be the case with some drugs.

Let us sum up in a few sentences what has been said in the last two chapters: (1) Vagotonia is a functional increase of tone in the autonomic system. (2) This increase may affect nearly all

or but a few of the branches. (3) The origin lies in a latent increase of function and this permits stimuli to act more readily than on a nervous system in which no such increase exists. (4) Vagotonics, therefore, are more responsive than individuals having a normal vegetative system.

8. COMBINATION OF VAGOTONIA WITH OTHER DISEASES

In the foregoing chapters we have attempted to show that many people have a constitutional condition which makes a visceral nerve—by this is to be understood the entire autonomic or extended vagus, more irritable than its antagonist, the sympathetic. When we consider that these two nerve plexuses control all visceral organs, we cannot fail to realize that a disturbance of one of them will produce anomalous conditions in many organs. On the one hand this constitutional condition may be regarded as stationary and as of long duration,—on the other hand, there are periods in which the condition will be exaggerated and more susceptible to irritation. This fact may well be correlated with the occurrence of various diseases at certain periods of life. We recognize various periods, which dispose to certain diseases, as old age, youth, climacterium, puberty, and menstruation, and we know that during these periods, certain groups of symptoms take the foreground. It seems worthy of question whether or not the constitutional state, which we have described, does not also influence certain diseases in a similar way. We have been able to show that spastic states in a limited part of the autonomic system occur in individuals having precisely this constitutional condition. Our attempt to draw other pathological conditions into correlation with the constitutional state we have described must not overshadow the fact that we do not intend to divide all individuals into two classes: the vagotonic and the sympathicotonic, but shall base whatever conclusions we may reach on cases in which there have been well-defined functional disturbances in two or three parts of the autonomic nervous system. Furthermore, the cases must have shown these disturbances not only before, but also after the disease. We hope to be able to show in what follows that those characteristics of a particular course of a disease, which heretofore have been ascribed to individual idiosyncrasy, are in reality due to a lack or excess of a definite nervous disposition of the organism.

Pain is the simplest example of the rôle which nervous components of a syndrome play in its symptomatology. In the same syndrome various individuals may have the intensity of a certain pain vary to a great degree. Certain individuals are not susceptible to the action of cocaine, and the admission that it has not acted in the right place must be made. Analogously, we must admit that poisons produced by certain diseases do not always act on the same parts of the body in each case. For this reason, certain very definite, well-known symptoms often are in the background, while others are so conspicuous that the classical picture of the disease is entirely effaced.

For example, should a vagotonic get a gastric ulcer of organic origin, one can readily see that the stimuli from the lesion will pass along the more readily irritable vagus. Thus we shall find in vagotonics with gastric ulcer, a hyperacidity and both increased tone and peristalsis of the stomach, combined with the symptoms they produce. Furthermore, cases of gastric ulcer will show signs of autonomic irritation in other parts than those directly affected. Thus we find bradycardia²⁸ as well as the cardinal symptoms of ulcer, hyperacidity, and great pain combined with retching and a tendency to spastic constipation. The symptoms may vary according to the locality of the ulcer. In some cases of ulcer one finds signs of hour-glass stomach. At operation or at autopsy this diagnosis is not confirmed.

When it is considered that X-ray signs of hour-glass stomach are found in simple vagotonics, there is no cause for wonder that when an ulcer exists, this can also occur, and that these signs of hour-glass stomach are due to an increased tone of the gastric musculature. This in turn is made clearer upon the basis of an increased tone in the autonomic system. On the other hand, it is known that there are cases of gastric ulcer in which no signs of gastric hyperacidity occur, and which are unaccompanied by pain, the only clue to their existence being the presence of occult blood in the stools. Some are found only at autopsy. It seems very significant that signs of general vagotonia are never found in such cases. Cases of gastric ulcer have been seen in which the hydrochloric acid value was not at all increased.

²⁸ Neusser, *Ausgewählte Kapitel der klinischen Symptomatologie und Diagnostic*, I H. 1904.

These constituted the most difficult group to diagnose from carcinoma, an observation of the greatest interest, since these are cases which tend to develop true neoplasms—callous ulcers. When these facts are considered the question arises whether the various clinical courses of such diseases as Cholangitis, Cholelithiasis and Nephrolithiasis are not in some way related to constitutional variations.

Certain cases of gall-stone disease particularly show symptoms which are due to autonomic stimulation. Since this exists not only before but also after the attack, the assumption of a latent constitutional disorder, which alters the course of disease, is well founded. Cholecystitis is often associated with hyperacidity. The vomiting and diarrhea may be referred to the attack, but all of these also presuppose a certain predisposing irritability of the organs involved. We believe that the spastic state, which begins in the gall-bladder and spreads thence to neighboring organs, causing vomiting or diarrhea, may also pass over into the gall passages. Only in this way is it possible to account for the transitory jaundice which occurs in cases of acute cholecystitis, in which there is no reason to believe that a stone is present to cause the jaundice mechanically. That the stone should be forced by the colic into the ductus choledochus and should then fall back after the colic is over, seems very improbable. Finally we wish to call attention to the inconstancy of the relation between bradycardia and jaundice in these cases and to the additional fact that the bradycardia may not exist in old people. In the young as well great variations may be observed, so that here, too, we must assume some predisposition of the cardiac vagus. If on the one hand, gastric ulcer and some cases of gall-stone colic are related to autonomic irritation, it would seem on the other hand that the diminished gastric acidity and mobility, and the dry skin and mucous membranes of carcinoma signified a diminution in the activity of the autonomic. In this connection it seems significant that we found that adrenalin glycosuria was almost never absent in the more severe types of general carcinomatosis, while pilocarpin never gave strong reactions. Thus the question is raised whether perhaps the nervous constitution does not play a rôle in the occurrence of tumors. The question also arises,—does the constitutional state of the individual cause

a definite course in such autonomic diseases of the nervous system as *tabes dorsalis*.²⁹

It is well known that there is a group of cases of this disease which begin with visceral disturbances, crises, as the most prominent symptoms, nor is it infrequent to find cases in which these crises are entirely lacking. It is not difficult to show that the crises themselves are signs of autonomic irritation. The narrowing of the pupil at the onset of the attack, the subsequent gastric hypersecretion,—sometimes associated with hyperacidity, the increased peristalsis and sweating, which may occur alone or at the height of some other crises, the epiphora, laryngeal and rectal crises, all show that at the height of the attack the autonomic is in a state of irritation. The fact that the spastic states are replaced in the later stages of the disease by their opposites (paralysis of the recurrent laryngeal, marked gastric and intestinal atony, anacidity, and even incontinence of feces and urine, impotence, etc.) leads us to believe that what were originally irritative states of the autonomic have been replaced by paralysis of those centers which originally caused the irritation. A proof of this for us is in the discovery that in many severe cases of *tabes*, degenerations were found in the trunk and nucleus of the vagus. It may be permitted us on these grounds to assume that the toxic agent of *tabes dorsalis*, in addition to attacking the posterior spinal cord columns, has also a specific affinity for the autonomic system, since it first irritates and then paralyzes it. It is difficult to say whether or not the crises, regarded as spastic states, are merely states of irritation superimposed upon vagotonia. It is, however, striking that cases without crises do not show signs of general vagotonia. A further argument in favor of our hypothesis is that those signs which are so often found associated with vagotonia, as for example, status thymicus and lymphatism were never found in cases of *tabes* without crises, since according to Edinger's theory of the consumption of neurotropic poisons, they first affect those nerves which are functionally most active, we might, by analogy, consider the possibility that the already over-irritable autonomic system would be most prone to take up the toxic agents of *tabes dorsalis*.

The following case may be taken as an example of the pre-

²⁹ Eppinger and Hess, *Wiener klin. Rundschau*, 1909, No. 47.

disposing affect, which pre-existing vagotonia has upon the occurrence of crises in tabes:

A. F., a merchant, has complained since his youth of nervous stomach trouble. He took soda for its relief. Fifteen years ago a gastric analysis was done and showed hyperacidity. He has been constive for many years, going to stool but every three to four days. The stool is very small in size, and often mixed with mucus. He has a tendency to salivate and sweat at the same time. Ten years ago the patient was infected with syphilis. This was followed by a course of mercurial inunctions. The first signs of gastric crises occurred over three years ago. Three years ago the symptoms increased so that he had continuous vomiting and marked gastric pains for two to three days of each week. Even when he had not taken food, the patient vomited large amounts of an acid, bile-stained fluid. As the increase in frequency of these attacks continued, the patient came to the clinic for advice. Objectively there were absence of the light-reflex, permanent absence of the knee-jerks, and a moderate anesthesia in the region of the right nipple. The "Head zone," corresponding to the stomach, showed marked hyperalgesia. During the crises, the blood pressure fell from the normal 105 mm. Hg. to 70 and even 60.

Basedow's disease is another example of the significance of vagotonia in understanding pathological conditions. It will be very difficult to account for all the symptoms of this disease on the basis of one cause, if one takes the point of view that they are referable to nerve irritation. Symptoms which are referable to sympathetic stimulation are found associated with others undoubtedly referable to autonomic stimulation. The cardinal symptoms themselves, exophthalmos and tachycardia on one hand, sweating and diarrhea on the other, indicate stimulation of both parts of the vegetative nervous system. In another article we have attempted to show that one explanation will not account for all the accessory symptoms, but that in the individual, both autonomic and sympathetic stimulation are combined, even though this may be but a transitory matter. On the other hand, we have found typical cases of Basedow's disease, in which all the symptoms were due to stimulation of one of the two nervous systems. The diagnosis in these cases was made certain by the increase in the level of metabolism shown by a marked degree of emaciation in spite of a sufficient diet. On the basis of these cases, we divided Basedow's disease into a vagotonic and a sympathicotonic type. Characteristic of the first type were: (1) relatively slight increase of the pulse rate, (2) subjective cardiac symptoms, (3) marked v. Gräfe's sign, (4) wide lid-slits, (5) absence of Moebius's sign, (6) very moderate grade of exophthalmos, (7) marked epiphora, (8) excessive sweating, (9) profuse diarrhea, (10) symptoms of gastric hyperacidity, (11) eosinoph-

ilia, (12) disturbances in the rhythm and mechanism of respiration, (13) absence of alimentary glycosuria.

In the sympathicotonic cases there were (1) marked exophthalmos, (2) no. v Gräfe's sign, (3) positive Löwi's phenomenon, (4) marked Moebius's sign, (5) frequently dry eyes, (6) a high degree of tachycardia with no subjective symptoms, (7) no sweating, (8) no diarrhea, (9) marked falling out of the hair, (10) tendency to rises in temperature, (11) no eosinophilia, (12) no respiratory disturbances, (13) alimentary glycosuria. We were able to establish the antagonism between adrenalin and pilocarpin in these cases. The number of cases in which one or the other system was excessively irritated was, however, very small. Those which were of the sympathetic type showed but little reaction to pilocarpin, while those which were of the vagotonic type showed no glycosuria after adrenalin. These types, which are not always constant, one passing into the other in various phases of the disease, led us to believe that at the root of the matter lay a difference in the make-up or constitution of the individual. By this we mean simply that those who are vagotonic before acquiring the disease, will be mainly of the vagotonic type during it, while those who were previously of the sympathicotonic type will have symptoms corresponding to those produced by sympathetic irritation. Furthermore, should the individual have been neither vagotonic nor sympathicotonic before the onset of the disease, the thyroid secretion, since it affects both symptoms, will cause symptoms of irritation of both.

It is worthy of mention that the one case, which was of the pure sympathetic type showed practically no thymus nor any lymphatic tissue. To this we would add that in another case, which had sympathetic symptoms for a long time, but developed in addition some vagotonic symptoms just prior to death, showed a large thymus and well-developed lymphatic system at autopsy. In spite of this, we believe that those who are vagotonics before acquiring a Basedow, will show during the disease the symptoms produced by the action of those components of the thyroid secretion, which acts upon the autonomic nervous system. By this we do not wish to imply a condition of dysthyroidism, but that these individuals do not react to those constituents of the thyroid secretions, which stimulate the sympathetic, just as certain individuals do not react to adrenalin. The fact that both at the

height of a severe case of Basedow and during the course of a very mild one there may exist severe symptoms of irritation of both systems may be interpreted as the weak point in our idea of their genesis, since we have advanced the viewpoint that if the vagus is strongly stimulated, it is scarcely possible that there should exist a simultaneous high degree of stimulation of the sympathetic.

Observations upon those afflicted with mental disease have shown that when it is most severe there is a disturbance of the equilibrium of the vegetative nervous system. Thus we can draw an analogy between Basedow's disease and central nervous system disease and say that where either exists the equilibrium will be disturbed. We observed that in many cases of catatonic or maniacal excitement there occur in quick succession strong glycosuric reactions to adrenalin, followed by marked responses to pilocarpin. We never saw so high a degree of glycosuria as in those having mental disease (early stage of dementia praecox), nor such marked responses to pilocarpin. After the usual dose of pilocarpin (gr. 1/6), some cases had such severe salivation and epiphora, besides a discharge from the nose, that there was almost a continual stream from both nose and mouth. These were the cases which, after the administration of pilocarpin, usually reacted with spermatorrhea, vomiting, severe sweating and urinary urgency.

We often found a reaction of both parts of the vegetative nervous system in diseases of the spinal cord, as multiple sclerosis or transverse myelitis.

The fact that during the psychic disturbances of mental disease over-irritability of both parts of the vegetative nervous system could be demonstrated, permits us to give the same fact more consideration in Basedow's disease.

In looking over our case histories we found that the group of cases, which showed alternately signs of irritation of the two systems were not complicated by mental disturbances, while those which showed these signs simultaneously often were complicated by psychical disturbances of one sort or another.

In investigating psychoses we found individuals who did not react to the usual dose of sympathicotrophic or vagotropic substances. Since these cases were mainly of the depressed type, we feel that our observations are of some significance in the consideration of the pathogenesis of certain psychoses.

The absence of central control may play a part in Basedow cases as well as it does in mental disease with excitement. This point of central control brings us naturally to the idea that under physiological conditions, the central nervous system exerts a definite influence over the antagonistic parts of the vegetative nervous system.

Several observations on conditions not typically Basedow's disease deserve mention. These conditions are of thyroid origin, but are not fully developed classical thyreopathies. They have been designated as "goitre heart," or as "Basedowoid Conditions" (Stern³⁰).

Since the symptoms of vagotonia (diarrhea, subjective palpitation, sweating, eye symptoms, tremor and general nervousness) are very similar to those of thyroid intoxication, the possibility must be advanced that certain questionable and atypical forms of thyroid disease may in reality be vagotonia. It is a frequent occurrence to diagnose Basedow's disease on the basis of one cardinal symptom,—as tachycardia—without determining the presence or absence of the main characteristic symptom,—increased metabolic exchange, with resultant loss of weight.

If this be made the crux of a diagnosis of Basedow's disease, it will be found that many cases of so-called incompletely developed Basedow's disease are in reality nothing but vagotonic neuroses. If these cases are operated upon it will be found that, as a rule, no good effect will be obtained, indeed there may be some aggravation of the disease. As to the symptomatic picture of cases of "goitre heart," we cannot fail to observe that the vagotonic picture is so conspicuous that there seems to be but a combination of vagotonia and goiter. The coëxistence of two pathological, constitutional states, vagotonia and endemic goiter, must be thought of particularly in neighborhoods where goiter is endemic and where Basedow's and hyperthyroidism are known to be relatively infrequent (as in Styria and certain Alpine districts).

Some observations must be made upon the changes at the climacterium. This state gives rise to many nervous symptoms; some of cardiac or vasomotor origin, some of gastro-intestinal and metabolic origin. Analogous to these are the withdrawal symptoms after castration, when vasomotor disturbances are also to be

³⁰ Stern, Differenzialdiagnose und Verlauf des Morbus Basedowii, Jahrbuch d. Psych. u. Neur., 1909, Vol. 29.

found. Not infrequently one finds that there is an enlargement of the thyroid at the climacterium or during pregnancy. It is a simple deduction to suppose that when vasomotor or visceral symptoms coëxist with thyroid enlargement, a similar disturbance exists in the relations of the endocrinous glands, as undoubtedly occurs in Basedow's disease. If one analyzes the symptoms of the climacterium, one finds it easy to relate them to the symptoms produced by stimulation of the autonomic nervous system. The symptoms include unaccountable sweating, v. Gräfe's sign, marked dermatographismus, hyperacidity, and hypersecretion, colic-like pains about the pyloric or gall tract region, and high sugar tolerance. Other symptoms, most frequently observed in vagotonia, are respiratory disturbances and cardiac pains, associated with symptoms like those of angina pectoris vasomotoria.

The metabolic change, the post-climacterial obesity, may be contrasted with the emaciation resultant upon sympathetic stimulation (adrenalin poisoning). As a general rule vagotonic stimuli are most often observed in youth. It is therefore a matter of surprise to find disturbances as gastrosucchoresis and pylorospasm in elderly men between forty-five and fifty-five. It would seem that men, like women, show symptoms of a climacterium, symptoms due to an absence of the sex-gland secretion, with consequent furtherance of autonomic stimulation.

Juvenile emphysema deserves a word of mention in connection with the relation of vagotonia to disease symptoms. Quite justly this disease is attributed to some disturbance of the respiratory mechanism. When the lung is distended for a considerable period by increase in the rate or the degree of inspiration, which almost exclusively serves the process of expiration, the passive contractile elastic apparatus is very materially overworked, and may eventually become insufficient. An increased tone of the bronchial musculature will make the expulsion of air by expiration difficult and will cause a lasting distention of the lung.

Analogous to this is the diminished power of the elastic elements of the lung to expel the alveolar air by expiration, a condition which develops upon a chronic asthma, or a chronic bronchitis, and is due to relative narrowness of the bronchial tree.

Investigations carried out with the spirometer and described in a previous section have shown that in these cases we have to do

with changes in the tone of the bronchial musculature. We maintain that increased tone in these muscles possibly aggravated by a coëxistent bronchitis, will, when combined with an insufficiency in the respiratory mechanism, pave the way for juvenile emphysema.

In confirmation of this theory, we would say that we have never failed to find signs of vagotonia in cases of juvenile emphysema. We have no clinical observations upon thymic asthma or laryngospasm of the newborn. It seems, however, that the mechanical element, compression by the thymus, is not the only factor in their production, but that nervous disturbances, perhaps related to the thymus secretion, play a rôle in their etiology. We would suggest atropin for their relief.

It is no less interesting to give some attention to the nervous element of certain skin diseases, particularly those involving the blood-vessels. We, ourselves, have only studied urticaria, and as far as this group is concerned we can state that vagotonic manifestations are very conspicuous. We found high grades of hyperacidity, greatly increased gastric tone, almost a pathological state of peristalsis, and in most instances, eosinophilia.

Sweating is frequently complained of and hyperidrosis and troublesome salivation often result from the administration of pilocarpin. These individuals do not react well to adrenalin, and have a high sugar tolerance.³¹

Bronchial asthma and urticaria are not infrequently associated. The gastric changes did not give rise to symptoms in our case, and were in the background. When we consider that the vasodilators are controlled by the autonomic nervous system, and that the dermatographism seen in vagotonics may develop into an urticaria, the parallelism between vagotonia and urticaria becomes very striking.

A few observations upon anaphylaxis seem pertinent to our subject. If one inject a small amount of horse serum, and repeat the injection after three weeks have elapsed, severe anaphylactic phenomena result: a general eruption, collapse, dizziness and vomiting. The newer researches on the subject have shown that the symptomatic phenomena of anaphylaxis are due to autonomic

³¹ *Translator's Note.*—This statement has not been borne out in our experience, since 1 c.c. of adrenalin has been found to dispel some urticarial ashes in an hour or less. (W. M. K.)

irritation, and that these phenomena may, in some animals at least, be relieved by atropin. These facts make it desirable, both for theoretical and practical reasons, to study the manifestations of anaphylaxis in vagotonic individuals particularly since we know that serum disease does not occur in all cases in which it might be expected. Isolated observations from various sources have been of great interest to us. For example, the injection of serum and particularly its re-injection in children who have been asthmatic or have had laryngeal spasm (spasmodic croup) has been found to be very dangerous. Since we feared acute anaphylaxis in our vagotonic patients, and wished to avoid the general symptoms which it produces, we gave our second injections subcutaneously, and only observed the occurrence of local changes. Of thirty cases taken at random, only three showed any signs of a reaction. These three were vagotonics. Immediately after the injection, a large papular elevation formed about the puncture in the skin. This grew steadily larger. In the course of the next twenty-four hours, a general and very irritating urticaria developed.

In those who were not vagotonic the greatest reaction seen was the local one and this was absent in many of the cases. Further study of this question seems to us to be very desirable, not only on account of the dangers of serum disease, but also on account of its prevention by atropin. This study would seem to promise most if applied to children.

That the symptom, fever, lies in close relation to sympathetic stimuli is readily seen. Adrenalin will cause a rise in temperature, and cocain, which increases the action of adrenalin, may, according to the researches of A. Fröhlich, cause fever.

There is also much evidence to show that the various vagotropic substances have a temperature-reducing action. We also know that certain of the antipyretics cause some vagotonic symptoms as sweating and lowered blood pressure.³²

It may be assumed that the relationship between vagotonia and fever is such that vagotonics will tend not to develop as high fever as those who are not vagotonics. It is well known that there are individual variations in the fever reaction in that some will develop a high fever after minor and insignificant infections.

³² *Translators' Note.*—See editorial, Jour. Amer. Med. Assn., Vol. 62, p. 302.

We may say that our study of vagotonics has not shown any parallelism between vagotonia and lessened tendency to develop fever. The only thing worth noting is a fact which has been mentioned before, *i. e.*, that those with sympathetic Basedow's have a greater tendency to rises in temperature than those of the vagotonic type. They are the group which react with high temperatures to mild infections. An attempt to prove a relationship between vagotonia and infection should certainly be made in the near future.

The clearest relations are those of tuberculosis. At the onset, many cases of tuberculosis show various signs of vagotonia, as a tendency to sweat, diarrhea, lowered blood pressure, stomach and intestinal disturbances. Furthermore, the pharmacological tests with adrenalin and pilocarpin showed that scarcely any case of tuberculosis reacts to the former, while they always react with typical symptoms to the latter. A group of cases, which showed no signs of Addison's disease, did, however, show an increased sugar tolerance. This raises the question as to whether the toxin of tuberculosis does not have a specific predilection for the chromaffin system. Corresponding with this idea are certain findings in the adrenals in severe forms of tuberculosis. Though these glands show neither microscopical nor macroscopical changes, functional tests show that they contain very little or no adrenalin. There is also evidence to prove that scrofula, which is related both to tuberculosis and the lymphatic constitution, is associated with an over-irritable autonomic system.

Later we shall deal more in detail with Addison's disease and its relation to the lymphatic constitution, since in it the vagotonic signs and symptoms are most clear cut and are undoubtedly due to an absence of the adrenalin producing organs.

At all events, our few observations upon infectious diseases will make it easier to establish upon an experimental basis the etiological relationship between the vegetative nervous system and the disposition to infection.

9. RELATIONS OF ENDOCRINOUS GLANDS TO VAGOTONIA

By vagotonia, we understand a lasting, tonic irritation in the realm of the autonomic system which maintains its end-organs in a state which very closely resembles that produced by electrical stimulation of the autonomic.

The analogue to this is sympathicotonia. This is dependent upon normal functioning of the adrenal glands and the entire chromaffin system. These groups of cells, which yield adrenalin for the entire body, and which may even, under certain circumstances, produce an excess of secretion, maintain the sympathetic end-organs in a state of tonic contraction so that but small sympathetic impulses suffice to produce a large effect.

Since the end-organs are in a continual state of oscillation, their activity going first in one direction, then in another, it is essential that the antagonists should keep each other from going to too great an extreme. The stimulus for one of the two systems (sympathetic) is known—adrenalin. We do not know its physiological antagonist—only substitutes for it. Though we know that adrenalin is the hormone which stimulates the sympathetic nervous system, we have no right to believe that it is the only stimulant. On the basis of physiological observations that all organs are under the influence of both nervous systems, we may assume that stimuli arise from all organs which have either a stimulating or inhibitory effect upon the two nervous systems. This does not imply that these stimuli must be entirely stimulatory or inhibitory—*i. e.*, that they stimulate or inhibit one or the other system in its entirety. It is most probable that the hormones arising in the various endocrinous glands show variations and that their interplay makes the final effect different from that of any one of them. Decreased or increased function of several of these endocrinous glands, whose secretion would neither be entirely absent nor entirely present, would naturally emphasize certain manifestations in some end-organs, manifestations which would be absent under other circumstances. An analogy from pharmacology may be found in the actions of physostigmin and curare. Physostigmin, though a vagotropic drug, cannot be entirely antagonized by curare. The general paralyzant action of curare may be counteracted by physostigmin (Rothberger).³³ The lack of irritability of the cardiac vagus after large doses of curare may be overcome by physostigmin. On the other hand, though curare has no paralyzing effect upon the stimulatory nerves of the sweat glands, physostigmin stimulates them very powerfully.

But let us return to general pathology.

³³ Rothberger, Pflüg. Arch., Vol. 87, p. 117, 1901.

The thyroid certainly contains sympathicotrophic substances, though they are not adrenalin. They differ from it in their action, for though the thyroid substances act upon the accelerators of the heart and upon metabolism, they exert but little influence upon vasoconstrictors.

In pituitrin, we have a blood-pressure raising substance, which however, also differs from adrenalin. There are, no doubt, more sympathicotrophic substances which differ both in their site of production and their action. These substances differ mostly in the intensity of their action: adrenalin stimulates the entire sympathetic nervous system. The other sympathicotrophic substances stimulate the same system, but only in certain of its parts.

It is to be expected that there should exist some hormone in the body which would be an antagonist to adrenalin, and in the light of this we must feel that there is an autonomin which has a selective action upon the autonomic system, just as adrenalin has upon the sympathetic.

However, we know neither its source nor its constitution. But a few substances are known which have a stimulating action upon some parts of the autonomic system. Thyroid stimulates the intestine, the sweat and salivary glands. Infundibulin seems to act only upon the pelvic nerve, leaving other branches unaffected. Formerly it was felt that in cholin, a substance present in every cellular organ of the body, there had been found the universal autonomin. When one considers, however, what large amounts of this substance are necessary to bring about stimulation of the autonomic, it, in contrast to adrenalin, seems very little likely to be able to play a prominent physiological part. Finally we must not omit to remark that substances may be isolated from various organs, which as far as their action upon blood-pressure goes, may be considered autonomic stimulants. The experiments with these substances seem to us not to be entirely reliable, since the substances were never obtained in the pure states. This leads one to believe that the action upon the autonomic system may have been due to the presence of peptone as an impurity. While physiology has yielded us no certain knowledge of any hormone except adrenalin, yet certain disease complexes give us a hint where autonomic stimulants are produced. It has been felt that extirpation experiments will show the way by which to approach the sought-for goal.

Up to now this method has only been of value in metabolic questions. On the basis of this method, it has been ascertained that the pancreas may be the site of production of autonomic stimulation. Its secretion probably acts in opposition to that of the chromaffin system, since when it is absent, the full action of the chromaffin hormone is felt, at least, as far as metabolism is concerned. Depancreatized dogs showed neither tachycardia nor increased blood-pressure. Only as far as the pupil is concerned are we certain of any increase in the tone of the sympathetic system. The thyroid must, as far as metabolism is concerned, furnish sympathicotrophic substance, since feeding thyroid causes an increase in metabolism as does adrenalinemia, and also favors alimentary glycosuria, *i. e.*, lowers sugar tolerance.

Lack of thyroid, on the other hand, increases tolerance for carbohydrates, and furthermore this tolerance may remain the same in spite of administration of adrenalin.

We could present many other facts which go to prove that the various organs produce sympathicotrophic and vagotonic impulses, but only those facts relative to metabolism can be presented, while the action upon the tone of smooth musculature and upon the activity of the other glands can scarcely be more than touched upon. We may expect by analogy to the action which we know is exerted upon metabolism by the glands of internal secretion, that they would also exert an inhibitory or stimulative action upon other vegetative functions.

The question now arises whether some clue may not be derived from general pathology, which may strengthen our idea that in the absence of certain endocrinous glands, there exists some condition analogous to vagotonia. The best example of this is Addison's disease, in which the organ from which sympathicotrophic impulses arise is absent. If we test the symptoms of this disease, we find the following: emaciation, diarrhea, lowered blood-pressure, pigmentation, sweating, general adynamia, high sugar tolerance and frequently hypoglycemia.

The diminution in blood-pressure and blood sugar is surely referable to the lessened activity of the chromaffin system. In addition there are conditions like those resultant upon autonomic stimulation: Sweating, diarrhea, which in comparison to their insignificance in the basic disease, tuberculosis, are very prominent. There are anatomical findings in typical Addison's disease

besides those in the adrenals, *i. e.*, a general lymphatic enlargement. The thymus also is enlarged, it being not only persistent in adults, but also not infrequently hyperplastic. The question of whether or not the thymus belongs to the lymphatic system will not be discussed in this paper. This fact must be added, that while the clinical picture of Addison's disease always is associated with diseased adrenals, diseased adrenals may not always cause a symptom-complex identical to Addison's disease. One is not infrequently astonished to find at autopsy that the adrenals are severely diseased, a diagnosis which could not be made *in vivo* due to the lack of any significant symptoms. And furthermore, every case does not show, at section, an enlarged lymphatic system and a hyperplastic thymus. Finally, adrenalin injections benefit the symptoms of Addison's disease.

This coincidence between adrenal disease and lymphatism or thymus hyperplasia was first observed in the cadaver by Wiesel,³⁴ Hedinger³⁵ and Hart.³⁶

These authors suggest that apparently primary lymphatism might be due to inferiority of the chromaffin system. Wiesel stated that the adrenalin-producing system was poorly developed just in that group of cases in which status thymicus was most marked. The question now arises, what knowledge concerning this relationship may be gained by considering the clinical and anatomic findings in Addison's disease. If the conception of vagotonia as the opposite to that constitutional state in which the adrenalin-producing organs dominate metabolism and smooth muscle activity be correct, there can be no doubt that Addison's disease may be considered as an exaggerated form of vagotonia.

Unfortunately our knowledge of the functions of the automatically innervated organs is as yet very scanty.

This we have been able to augment a little. Besides we must not overlook the probable effects of a state of inanition, such as found in Addison's, particularly upon the functions which the smooth muscles subserve. Thus we never have a truly clear-cut picture. But in spite of this the symptoms of vagotonia are so

³⁴ Wiesel, J., *Virchow's Archiv.*, 176, p. 103, 1904; *Beiträge zur pathol. Anatomie und allg. Pathologie*, 37, p. 168, 1904.

³⁵ Hedinger, *Verhandl. der XI Tagung der Deutschen pathol. Gesellschaft*, p. 29, 1907. *Frankfurter Zeitsch. f. Pathologie*, 1, p. 527, 1907.

³⁶ Hart, *Weiner klin. Wochenscht.*, 21, p. 1119, 1908. *Zentralblatt für die Grenzgebiete der Medizin und Chirurgie*, 12, p. 321, 1909.

outspoken in Addison's disease that we must of necessity regard it as a general secondary vagotonia. In spite of the inanition, hyperacidity and evidence of increased gastric tonus are not infrequently found in Addison's. The enormous development of the lymphatic tissue and the frequency of thymus hyperplasia, found in autopsy, in those who have died of Addison's, and similar findings in those who clinically were vagotonics, lead us to believe that a relationship exists and that perhaps the manifestations of vagotonia are related to the pathological conditions in the thymus and the marked enlargement of the lymphatic tissues.

We shall now try to present some basis for this idea:

We have frequently observed that vagotonia occurs most often in young people. Experimental pathology also has taught us that a higher vagal tone is to be expected in young animals than in adults. Furthermore, according to Bartel,³⁷ lymphatism is found with decreasing frequency as age increases. Since we know that the thymus disappears after a certain age, while in youth it is almost a physiological organ, the above-mentioned facts cannot fail to be both striking and noteworthy. We believe also that we can derive some additional proof from Graves' disease, which is so often associated with a persistent thymus. We have learned from the researches of Tacher that in Graves' disease an accumulation of lymphoid tissue occurs in the thyroid and in the more usual places, where this type of cell is found. Further that this is more pronounced the longer the duration of the disease has been. This suggested the hypothesis that a substitution or healing process was taking place, the lymph tissue growing to replace some diminution in the activities of some other organ. This idea had been advanced by earlier authors. Mikulicz recommended thymus preparations in the treatment of Basedow's disease, and his reports leave the impression that some good was done by its administration. We ourselves have noted that lymphatism and the signs of persistent thymus were most pronounced in the markedly vagotonic forms of Basedow's disease. And it is of further interest that our vagotonic showed an eosinophilia and relative lymphocytosis,

³⁷ Bartel, J., Über Konstitution und Krankheit. Verhandlungen der Deutschen pathologischen Gesellschaft, 1910, 14 Tagung.

the same as in the vagotonic Basedow cases. Recently Bartel³⁸ has studied the question of status thymicolymphaticus from the anatomic point of view.

He concludes that lymphatism and persistent thymus are part of a general state of inferiority, one of whose manifestations is a decreased resistance to many noxious influences. What interests us most, however, is the coincidence of lymphatism with just that group of diseases which we ourselves have found associated with vagotonia. He finds, for example, that certain diseases are never associated with a lymphatism, while in others it is a frequent finding. It is of special significance that Bartel never found carcinoma and lymphatism associated, while cases with sarcoma, a disease of youth, frequently showed lymphatism as well.

He proposes the theory that there exists in the constitutional inferiority of status thymicolymphaticus some factor which predisposes to certain diseases and against others. Now the fact is that just those diseases which we have found to be vagotonic in nature, or which are readily developed upon a vagotonic basis, are, according to Bartel's findings, combined with lymphatism. This may be shown in part by clinical observations. We have shown that in many cases of vagotonics there is enlargement of those parts of the lymphatic system which are enlarged in status thymicolymphaticus. More accurate proof we have not, since this proof is based on anatomical findings. Probably the anatomical entity status thymicolymphaticus corresponds most closely to the clinical entity, exudative diathesis, which Czerny has described. But there is great difficulty in determining this clinical entity anatomically, since in children it is difficult to set a limit between normal and enlarged lymph tissue. Clinically Czerny's exudative diathesis corresponds most closely to vagotonia. One may even go so far as to say that the exudative diathesis, with its tendency to spastic states and convulsions, to vascular disturbances and exudations, is but an infantile form of vagotonia. It is greatly to be desired that pediatricians should aid us by an analysis of the symptoms found in children with exudative diathesis. Our theory is much strengthened by Strümpell's observation that those who are affected with bron-

³⁸ Bartel, J., "Über die hypoplastische Constitution und ihre Bedeutung," Wiener klin. Woch., 1908, No. 22.

chial asthma are, perhaps, of the class who have had the exudative diathesis in childhood.

It may be seen that we have found in our conception of vagotonia a way to discover in various types of individuals a definite constitutional state, which in some cases may predispose to disease, in others may give a disease a definite course. This has given a degree of unity to phenomena which hitherto have been considered both clinically and anatomically as due to various kinds of predisposition.

The criterion, which clinicians and anatomists have used to describe the origin of these predispositions, has up to now been only morphological. The important thing has been the lymphatic tissues, and their reaction to various stimuli. Nothing could be said of the function of this reaction, except that it was associated with some degree of constitutional inferiority.

Since statistical studies have shown that length of life as well as morbidity are closely related to these morphological changes, one may say that lymphatism, combined with status thymicus, comprise a remarkable constitutional state of inferiority, and is related to a predisposition to certain definite diseases.

Our attempt to determine a form of predisposition by functional tests of a chemical nature brings up the very interesting question, is there any parallelism between a clinical and anatomic predisposition? In our opinion this parallelism may be doubly demonstrated. Just as Bartel states that lymphatism is a partial manifestation of constitutional inferiority, and is frequently associated with developmental anomalies, so do we believe that vagotonia is a partial manifestation of an inferior organism. We feel that the chromaffin organs, like other organs may be arrested in their development. Thus adrenalin would be produced in lesser amounts, and its antagonist would take the upper hand. This should be considered particularly in cases of general vagotonia.

There are many clinical proofs that defective development of the adrenals, and thus their functional activity, plays an important part. We find that cases of vagotonia have enteroptosis, are of the degenerate type of individual, and frequently have neurasthenia, hysteria, high arched palates, flat foot and syndactily in association with the symptoms of the vagotonia.

We must also consider the possibility that vagotonia, which

improves with advancing age, and in fact may even disappear, and yet, under certain pathological conditions may reappear, may be closely related to an overactivity of some of the glands of internal secretion. Thus a state would be produced by this change in the interrelations of the glands of internal secretion, which could certainly not be considered an anatomic form of constitutional inferiority.

We feel that vagotonia may very probably be the clinical component of the anatomical lymphatic constitution.

The parallelism between the clinical picture of status thymicolymphaticus, uncertain though it may be, and the readily demonstrable anomalies of vagotonia, makes us very prone to believe our theory of their relation to be true. The fact that we could not give a clinical demonstration of status thymicolymphaticus in many of our vagotonic cases, is not weighty evidence against our theory, since status thymicolymphaticus may only be demonstrated anatomically. Furthermore, it is unusual to have a typical vagotonic come to autopsy, since vagotonia occurs most usually in the youthful. Yet we were able in a few cases to confirm the parallelism of vagotonia and status thymicolymphaticus at autopsy. We hope to be able to demonstrate this experimentally.

In closing, we wish to say a word about the etiology of the mixed forms of vagotonia. Perhaps these are due to a polyglandular disturbance of endocrinous nature. Thus the picture of vagotonia would be obscured. Just as the typical action of physostygmmin is obscured by using curare with it. At all events, these cases offer a very fertile field for clinical study.

10. THERAPEUTIC OBSERVATIONS

Our attempt at the close of our article to outline therapeutics leads us first to emphasize one point, that therapeutic measures which we shall recommend are not directed against vagotonia as a constitutional condition, but against those symptoms of irritation in the autonomic system, which may be considered as irritative states superimposed upon the constitutional condition.

Atropin is the best antidote for the spastic states. It is of therapeutic value, as well as diagnostic value, and should be tried in all diseases, due to or associated with vagotonia. Not only is

its paralyzing action of value, as a therapeutic agent against symptoms, but it may also be of value in combating the etiological factor. It may be used to great advantage in bronchial asthma, in which small doses may be used without danger for many weeks. It should be given in doses of one to two milligrams a day, subcutaneously. In the course of the treatment, this may be increased to three milligrams, after which the former dosage is resumed.

Another group of conditions, in which atropin is very useful, is that relating to vagotonic gastric disturbances, gastric ulcer (Tabora) and hyperacidity, as well as gastric crises. The addition of atropin is often required, when gastric disturbances follow the use of the infusion of digitalis. Atropin is also of great value in treating cardiac conduction disturbances, as well as the troublesome subjective symptoms of extrasystolic arrhythmias.

The harmlessness of atropin demands that it be used more extensively than hitherto. Atropin should be tried if, combined with those varied obscure and troublesome complaints, which, due to lack of anatomic basis, are called "nervous," a patient is found with signs of a vagotonic constitution. There is no need of discussing at length those substances which contain atropin, as belladonna and eumydrin. The latter has been used to advantage in the night sweats of tuberculosis.

If it is certain that the pathological condition to be treated is caused by vagotonic stimulation or irritation, and it is found that atropin is not a benefit, indeed may make the condition worse, the reason is that the dosage has been too small. We feel that atropin is but a substitute for some physiological "atropin" which is circulating in the body. The limitations of its use are that it does not affect all branches of the autonomic system equally—the pelvic nerve being but slightly affected.

The beneficial effect of adrenalin in many spastic states of the autonomic system (bronchial asthma, many forms of gall-stone colic, diarrhea) is a good proof that both symptomatically and etiologically vagus paralysis and sympathetic stimulation are closely allied.

II. CLOSING REMARKS

The value of the researches, which have been presented, should be many-sided. Above all, we believe that we have

paved the way for a new subject, *the neurology of visceral organs*. When one stops to consider to what degree the pathology of the peripheral nervous system has been developed, it must be a source of shame to the internist that he must admit that there scarcely exists a pathology of the nervous system of visceral organs worthy of the name. The main reason for this up to now has been the scanty knowledge of the physiology of the nervous system, one which at best is hard to understand. We know full well that many of the things, which we have stated, stand but on unsteady ground, but, in spite of this, we hope to have given the impetus to further investigations, which may be of great significance for special pathology and therapy.

In many instances, we have been able to draw conclusions from known physiological reactions, in many we have been constrained to study physiological reactions first, since the diseases, in which we were interested, had not themselves been authoritatively worked out.

Much light will undoubtedly be thrown upon pathology, if we consider it in the light of the physiology of the visceral nervous system. We have attempted to describe a state of increased irritation in the domain of the extended vagus on the basis of the differentiation of the autonomic and sympathetic nervous systems. We did not attempt at first to determine whether the action was predominatingly central or peripheral, but only that under certain circumstances the one system reacted to stimuli which in normal physiological states would scarcely be appreciable to a greater degree, and with more intensity than under normal conditions.

The name of *vagotonia* was chosen to describe this state when it occurred in the entire autonomic system. And it was shown by clinical observations to be a constitutional anomaly of no great infrequency. It seemed worth the while, also, to show that this nervous state of a certain class of individuals was not infrequently to be reckoned with in the various conditions of disease. Thus, many cases which until now have been described as intestinal neuroses could be shown to be identical with vagotonia, or at least vagotonia may be considered responsible for the course and symptoms of the condition.

We have tried to show, furthermore, that many diseased states are associated with autonomic stimulation, and that the possi-

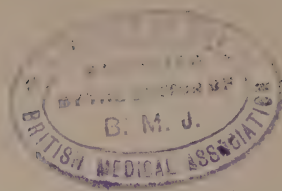
bility existed that a constitutional tendency of the organism, to react in a definite way to such stimulation might lie at the root of the matter. We not only believe that due to this constitutional make-up, the vagotonic reacts differently from a normal person to spastic states, but that vagotonia may be manifested symptomatically in almost all states of disease. When we stop to consider that almost every function of the intestine, and perhaps metabolism, in addition, are under the control of the autonomic nervous system, it is not difficult to see that an increased irritability of these visceral regulators, combined with the continuous flow of vagotonic influences, must be of great import in the course, not only of physiological, but also of pathological processes.

The real etiology of vagotonia must be sought in some disturbance of the internal secretions. Not only has an insufficiency of the chromaffin system been proved to exist in certain types of endocrinopathic individuals, but it has also been shown that these same individuals have a lymphatic system which is more strongly developed than normally.

When we consider that vagotonia exists more markedly in the young we may readily feel that some relation exists between it and status thymicus and the lymphatic constitution.

We feel also that vagotonia is the expression of an inferior constitutional make-up. As proof of this assumption we have our findings of the frequent coincidence of vagotonia, with states undoubtedly due to constitutional inferiority of the organism.

At any event, the investigations which have been presented in the foregoing pages demand that the future yield more research upon the subject of visceral neurology.



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